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Disease management interventions for heart failure (Review)

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[Intervention Review]

Disease management interventions for heart failure

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ABSTRACT

Background

Despite advances in treatment, the increasing and ageing population makes heart failure an important cause of morbidity and death worldwide. It is associated with high healthcare costs, partly driven by frequent hospital readmissions. Disease management interventions may help to manage people with heart failure in a more proactive, preventative way than drug therapy alone. This is the second update of a review published in 2005 and updated in 2012.

Objectives

To compare the effects of different disease management interventions for heart failure (which are not purely educational in focus), with usual care, in terms of death, hospital readmissions, quality of life and cost-related outcomes.

Search methods

We searched CENTRAL, MEDLINE, Embase and CINAHL for this review update on 9 January 2018 and two clinical trials registries on 4 July 2018. We applied no language restrictions.

Selection criteria

We included randomised controlled trials (RCTs) with at least six months' follow-up, comparing disease management interventions to usual care for adults who had been admitted to hospital at least once with a diagnosis of heart failure. There were three main types of intervention: case management; clinic-based interventions; multidisciplinary interventions.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Outcomes of interest were mortality due to heart failure, mortality due to any cause, hospital readmission for heart failure, hospital readmission for any cause, adverse effects, quality of life, costs and cost-effectiveness.

Main results

We found 22 new RCTs, so now include 47 RCTs (10,869 participants). Twenty-eight were case management interventions, seven were clinic-based models, nine were multidisciplinary interventions, and three could not be categorised as any of these. The included studies were predominantly in an older population, with most studies reporting a mean age of between 67 and 80 years. Seven RCTs were in upper-middle-income countries, the rest were in high-income countries.

Only two multidisciplinary-intervention RCTs reported mortality due to heart failure. Pooled analysis gave a risk ratio (RR) of 0.46 (95% confidence interval (CI) 0.23 to 0.95), but the very low-quality evidence means we are uncertain of the effect on mortality due to heart failure. Based on this limited evidence, the number needed to treat for an additional beneficial outcome (NNTB) is 12 (95% CI 9 to 126).

Twenty-six case management RCTs reported all-cause mortality, with low-quality evidence indicating that these may reduce all-cause mortality (RR 0.78, 95% CI 0.68 to 0.90; NNTB 25, 95% CI 17 to 54). We pooled all seven clinic-based studies, with low-quality evidence suggesting they may make little to no difference to all-cause mortality. Pooled analysis of eight multidisciplinary studies gave moderate-quality evidence that these probably reduce all-cause mortality (RR 0.67, 95% CI 0.54 to 0.83; NNTB 17, 95% CI 12 to 32).

We pooled data on heart failure readmissions from 12 case management studies. Moderate-quality evidence suggests that they probably reduce heart failure readmissions (RR 0.64, 95% CI 0.53 to 0.78; NNTB 8, 95% CI 6 to 13). We were able to pool only two clinic-based studies, and the moderate-quality evidence suggested that there is probably little or no difference in heart failure readmissions between clinic-based interventions and usual care (RR 1.01, 95% CI 0.87 to 1.18). Pooled analysis of five multidisciplinary interventions gave low-quality evidence that these may reduce the risk of heart failure readmissions (RR 0.68, 95% CI 0.50 to 0.92; NNTB 11, 95% CI 7 to 44).

Meta-analysis of 14 RCTs gave moderate-quality evidence that case management probably slightly reduces all-cause readmissions (RR 0.92, 95% CI 0.83 to 1.01); a decrease from 491 to 451 in 1000 people (95% CI 407 to 495). Pooling four clinic-based RCTs gave low-quality and somewhat heterogeneous evidence that these may result in little or no difference in all-cause readmissions (RR 0.90, 95% CI 0.72 to 1.12). Low-quality evidence from five RCTs indicated that multidisciplinary interventions may slightly reduce all-cause readmissions (RR 0.85, 95% CI 0.71 to 1.01); a decrease from 450 to 383 in 1000 people (95% CI 320 to 455).

Neither case management nor clinic-based intervention RCTs reported adverse effects. Two multidisciplinary interventions reported that no adverse events occurred. GRADE assessment of moderate quality suggested that there may be little or no difference in adverse effects between multidisciplinary interventions and usual care.

Quality of life was generally poorly reported, with high attrition. Low-quality evidence means we are uncertain about the effect of case management and multidisciplinary interventions on quality of life. Four clinic-based studies reported quality of life but we could not pool them due to differences in reporting. Low-quality evidence indicates that clinic-based interventions may result in little or no difference in quality of life.

Four case management programmes had cost-effectiveness analyses, and seven reported cost data. Low-quality evidence indicates that these may reduce costs and may be cost-effective. Two clinic-based studies reported cost savings. Low-quality evidence indicates that clinic-based interventions may reduce costs slightly. Low-quality data from one multidisciplinary intervention suggested this may be cost-effective from a societal perspective but less so from a health-services perspective.

Authors' conclusions

We found limited evidence for the effect of disease management programmes on mortality due to heart failure, with few studies reporting this outcome. Case management may reduce all-cause mortality, and multidisciplinary interventions probably also reduce all-cause mortality, but clinic-based interventions had little or no effect on all-cause mortality. Readmissions due to heart failure or any cause were probably reduced by case-management interventions. Clinic-based interventions probably make little or no difference to heart failure readmissions and may result in little or no difference in readmissions for any cause. Multidisciplinary interventions may reduce the risk of readmission for heart failure or for any cause. There was a lack of evidence for adverse effects, and conclusions on quality of life remain uncertain due to poor-quality data. Variations in study location and time of occurrence hamper attempts to review costs and cost-effectiveness.

The potential to improve quality of life is an important consideration but remains poorly reported. Improved reporting in future trials would strengthen the evidence for this patient-relevant outcome.

PLAIN LANGUAGE SUMMARY

Disease management programmes for heart failure

Review question

We investigated the effects of disease management programmes on death from heart failure or from any cause, hospital readmissions for heart failure or for any cause, adverse effects, quality of life and cost-effectiveness, in adults who had been admitted to hospital at least once for heart failure.

Background

Heart failure affects a person’s quality of life, is a frequent cause of hospital admission and has a high risk of death. Traditional drug therapy is the main treatment, but people may benefit from additional support from disease management programmes that aim to provide ongoing support rather than crisis management. Such programmes may be run by specialist nurses, as clinic-based interventions, or

by multidisciplinary teams. Community-based support of this kind could help to keep people out of hospital by improving day-to-day symptom management and providing an 'early warning system' for changes requiring medical attention.

Selection criteria

We conducted a comprehensive search for all studies investigating heart failure-specific disease management interventions for adults who had been admitted to hospital at least once for heart failure (evidence current to 9 January 2018).

Results and conclusions

We included 47 studies, with a total of 10,869 participants. Twenty-eight studies were case management interventions, seven were clinic-based models, nine were multidisciplinary interventions and three could not be categorised as any of these. The average age of the people in most of the studies was between 67 and 80 years old, although 10 studies had younger participants on average, and one included mostly very elderly people. Most trials were in Europe and North America, but others took place in China, Taiwan, Iran and Japan.

We found limited evidence for an effect on mortality due to heart failure, as few studies reported this outcome. There was some evidence that case management may reduce all-cause mortality, and multidisciplinary interventions probably do, but clinic-based studies appeared to have little or no effect on this. Readmissions due to heart failure and due to any cause were probably reduced by case management interventions. Clinic-based interventions probably make little or no difference to heart failure readmissions and may result in little or no difference in readmissions for any cause. Multidisciplinary interventions may reduce the risk of readmission for heart failure or any cause.

Only two studies mentioned adverse events, both stating that none occurred. Many studies measured quality of life, but it is difficult to draw conclusions for any effect because they tended to report this in different ways and did not report it for all their participants. Data on costs and cost-effectiveness were limited, but indicated a slight benefit of disease management programmes, mostly due to reduced hospital readmission costs.

Quality of the evidence

The quality of evidence was very low for mortality due to heart failure, low to moderate for all-cause mortality, low to moderate for heart failure readmissions, and all-cause readmissions, moderate for adverse events (where available), low to very low for quality of life and low to moderate for costs. The quality of evidence is important as it impacts on how certain we can be in the effect of the intervention on the outcomes we are interested in. For example, if the evidence is of very low quality, we cannot be certain of the intervention's effect.

Summary of findings for the main comparison. Case management compared to usual care for heart failure

Case management compared to usual care for heart failure

Patient or population: adults with heart failure
Setting: community
Intervention: case management
Comparison: usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual care	Risk with case management				
HF mortality	-	-	-	-	-	Not reported
All-cause mortality Follow-up: median 12 months	Study population 187 per 1000	146 per 1000 (127 to 168)	RR 0.78 (0.68 to 0.90)	6903 (26 RCTs)	⊕⊕⊖⊖ Low[1,2]	Case management may reduce all-cause mortality. NNTB 25 (95% CI 17 to 54)
HF readmissions Follow-up: median 12 months	Study population 361 per 1000	231 per 1000 (191 to 282)	RR 0.64 (0.53 to 0.78)	2528 (12 RCTs)	⊕⊕⊕⊖ Moderate[3]	Case management probably reduces HF readmissions: NNTB 8 (95% CI 6 to 13). 3 additional studies had data that could not be included in the meta-analysis
All-cause readmissions Follow-up: median 10.5 months	Study population 491 per 1000	451 per 1000 (407 to 495)	RR 0.92 (0.83 to 1.01)	4539 (14 RCTs)	⊕⊕⊕⊖ Moderate[4]	Case management probably reduces all-cause readmissions slightly: NNTB 26 (95% CI NNTH 204 to NNTB 12). 6 additional studies had data that could not be in-

					cluded in the meta-analysis
Adverse effects	-	-	-	-	None of the included studies reported adverse effects
Quality of life (MLHFQ mean score at end of follow-up) Follow-up: median 6 months	Analysis 1.13 includes 8 studies, six of which show a broadly positive effect of case management interventions, however, 2 small studies indicate that QoL may actually be lower in the case management groups. High heterogeneity precludes pooling these studies in a meta-analysis. 3 other studies also reported MLHFQ but for unclear or reduced numbers of participants. There was little evidence for any difference between groups in studies that did not report MLHFQ, but only used the EQ-5D, SF-8, SF-36 or KCCQ tools.	-	1595 (8 RCTs)	⊕⊖⊖⊖ Very low[5,6,7]	A lower score indicates better quality of life on the MLHFQ. We are uncertain about the effect of case management on QoL.
Costs and cost-effectiveness Follow-up: median 6 months	Cost-effectiveness analyses of 3 interventions generally suggest small CE benefits over usual care, but another one reported a cost of EUR 3746 per QALY gained with case management compared with usual care. 7 case management studies reported the costs of their programmes, although the wide range in dates and locations of studies complicates interpretation: 2 reported higher costs for intervention groups; 4 reported lower costs (generally after taking readmission costs into account); and 1 reported no difference in costs.	-	2369 (11 RCTs)	⊕⊕⊖⊖ Low[8,9]	Case management may reduce costs and improve cost-effectiveness slightly

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CE: cost-effectiveness; **CI:** confidence interval;**HF:** heart failure; **MLHFQ:** Minnesota Living with Heart Failure Questionnaire; **NNTB/H:** number needed to treat for an additional beneficial/harmful outcome; **QALY:** quality-adjusted life year; **QoL:** quality of life; **RCT:** randomised controlled trial; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]We could include only 11 of the 26 studies in the sensitivity analysis, and this showed a stronger positive effect than the main analysis. Downgraded once for risk of bias.
[2]Funnel plot is slightly asymmetric. Downgraded once for possible publication bias.
[3]Funnel plot is asymmetric and suggests publication bias - downgraded by one level.
[4]Confidence Interval includes the null as well as a small effect. Downgraded once for imprecision.
[5]Unclear or high risk of attrition bias for majority of studies for this outcome. Study was not blind and this outcome was self-assessed. Downgraded by two levels for risk of bias.

[6]High heterogeneity, and although subgroups differ, there remains high heterogeneity in 6-month follow-up studies. Downgraded once for inconsistency.
[7]Downgraded once for imprecision as reported results vary widely.
[8]Only 4 studies had cost-effectiveness analysis; 7 others reported costs which were hard to generalise. Downgraded once for indirectness of evidence.
[9]There was variation in the direction of effect for cost studies. Downgraded once for inconsistency.

Summary of findings 2. Clinic-based intervention compared to usual care for heart failure

Clinic-based intervention compared to usual care for heart failure

Patient or population: adults with heart failure
Setting: heart failure clinic (outpatients, community)
Intervention: heart failure clinic
Comparison: usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual care	Risk with clinic-based intervention				
HF mortality	-	-	-	-	-	Not reported
All-cause mortality Follow-up: median 12 months	Study population 273 per 1000	238 per 1000 (186 to 300)	RR 0.87 (0.68 to 1.10)	1686 (7 RCTs)	⊕⊕⊖⊖ Low[1,2]	Clinic may result in little to no difference in all-cause mortality. NNTB 29 (95% CI NNTH 37 to NNTB 12)
HF readmissions Follow-up: median 18 months	Study population 345 per 1000	348 per 1000 (300 to 407)	RR 1.01 (0.87 to 1.18)	887 (2 RCTs)	⊕⊕⊕⊖ Moderate[3]	Clinic probably results in little to no difference in HF readmissions. NNTH 290 (95% CI NNTH 17 to NNTB 23)
All-cause readmissions Follow-up: median 15 months	Study population 549 per 1000	494 per 1000 (395 to 615)	RR 0.90 (0.72 to 1.12)	1129 (4 RCTs)	⊕⊕⊖⊖ Low[2,4]	Clinic may result in little to no difference in all-cause readmissions. NNTB 19 (95% CI NNTH 16 to NNTB 7)
Adverse effects	-		-	-	-	Not reported

Quality of life Follow-up: median 12 months	1 study reported no difference in MLHFQ between groups at 1 year, and another reported similar changes from baseline for both intervention and control groups. 2 studies used the Nottingham Health Profile (NHP) rather than the MLHFQ, both reporting similar scores in intervention and control groups.	-	641 (4 RCTs)	⊕⊕⊖⊖ Low[5]	A lower score indicates better quality of life on both the MLHFQ and NHP. Clinic may result in little to no difference in quality of life.
Costs and cost-effectiveness Follow-up: range 6 months to 12 months	1 study reported a cost saving of EUR 1382 per person, the other a saving of USD 1300 per person	-	390 (2 RCTs)	⊕⊕⊖⊖ Low[6,7]	Clinic may reduce costs slightly.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **HF:** heart failure; **MLHFQ:** Minnesota Living with Heart Failure Questionnaire; **NNTB/H:** number needed to treat for an additional beneficial/harmful outcome; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]Sensitivity analysis included only 2 small studies at low risk of bias and showed more positive effect estimate but with much wider confidence interval. Downgraded by one level for risk of bias.
[2]Wide confidence interval includes null but not an important harm. Downgraded by one level for imprecision.
[3]Both studies were at unclear risk of bias for concealment of allocation, and one was also at unclear risk for randomisation method. Downgraded by one level for risk of bias.
[4]Only 1 small study was at low risk of bias for key domains. Downgraded by one level for risk of bias.
[5]Unblinded self-assessment of this subjective outcome. One study only collected data from fewer than half of the participants and the number of people providing data is unclear for another study. Downgraded by two levels for risk of bias.
[6]Costs reported but not cost-effectiveness. Age of one of the studies limits the generalisability of this. Downgraded by one level for indirectness of evidence.
[7]Small sample size. Downgraded by one level for imprecision.

Summary of findings 3. Multidisciplinary disease management programmes compared to usual care for heart failure

Multidisciplinary disease management programmes compared to usual care for heart failure

Patient or population: adults with heart failure
Setting: community

Intervention: multidisciplinary disease management programmes
Comparison: usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with usual care	Risk with multidisciplinary disease management programmes				
HF mortality Follow-up: median 12 months	Study population 159 per 1000	73 per 1000 (37 to 151)	RR 0.46 (0.23 to 0.95)	277 (2 RCTs)	⊕⊖⊖⊖ Very low[1,2,3]	We are uncertain about the effect of multidisciplinary disease management programmes on HF mortality. NNTB 12 (95% CI 9 to 126)
All-cause mortality follow-up: median 12 months	Study population 185 per 1000	124 per 1000 (100 to 154)	RR 0.67 (0.54 to 0.83)	1764 (8 RCTs)	⊕⊕⊕⊖ Moderate[4]	Multidisciplinary disease management programmes probably reduce all-cause mortality. NNTB 17 (95% CI 12 to 32)
HF readmissions Follow-up: median 12 months	Study population 290 per 1000	197 per 1000 (145 to 267)	RR 0.68 (0.50 to 0.92)	1108 (5 RCTs)	⊕⊕⊖⊖ Low[5,6]	Multidisciplinary disease management programmes may reduce HF readmissions. One study reported data that could not be included in the meta-analysis. NNTB 11 (95% CI 7 to 44)
All-cause readmissions Follow-up: median 12 months	Study population 450 per 1000	383 per 1000 (320 to 455)	RR 0.85 (0.71 to 1.01)	1152 (5 RCTs)	⊕⊕⊖⊖ Low[7,8]	Multidisciplinary disease management programmes may slightly reduce all-cause readmissions. 2 additional studies reported data that could not be included in the meta-analysis. NNTB 15 (95% CI NNTH 223 to NNTB 8)
Adverse effects Follow-up: range 6 to 12 months	2 multidisciplinary intervention trials mentioned that there were no adverse effects, or no major side effects, in either study arm.		-	496 (2 RCTs)	⊕⊕⊕⊖ Moderate[9]	Multidisciplinary disease management programmes probably result in little to no difference in adverse effects.

Quality of life (MLHFQ) Follow-up: median 12 months	1 study reported score at end of follow-up (34.3 in usual-care group). 1 study reported a decrease from baseline of 0.5 in usual-care group	MD 12.21 lower (16.43 lower to 7.99 lower) 1 study reported score at end of follow-up (19.4 in intervention group). 1 study reported a decrease from baseline of −11 in intervention group	-	140 (2 RCTs)	⊕⊖⊖⊖ Very low[10,11]	A lower score indicates better quality of life on the MLHFQ. 4 other studies used the MLHFQ but did not report data in a form that could be included in the meta-analysis. 1 study reported the KCCQ tool but not the MLHFQ. Overall, we are uncertain whether multidisciplinary disease management programmes affect quality of life.
Costs and cost-effectiveness Follow-up 12 months	Only 1 multidisciplinary intervention study reported costs or cost-effectiveness. In Gonzalez-Guerrero 2014, the cost per additional QALY for the disease management programme compared with usual care was EUR 38,274 from a healthcare perspective and EUR 25,390 from a societal perspective.		-	117 (1 RCT)	⊕⊕⊖⊖ Low[12,13]	Multidisciplinary disease management programmes may be cost-effective from a societal perspective but less so from a healthcare perspective.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: confidence interval; **HF:** heart failure; **KCCQ:** Kansas City Cardiomyopathy Questionnaire; **MLHFQ:** Minnesota Living with Heart Failure Questionnaire; **NNTB/H:** number needed to treat for an additional beneficial/harmful outcome; **QALY:** quality-adjusted life year; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

[1]The intervention for one of the studies (Gonzalez-Guerrero 2014), took place in a geriatric day care hospital. Whilst this was characterised as multidisciplinary due to the nature of care, it may not be fully characteristic of the more usual multidisciplinary intervention. Downgraded by one level for indirectness.
[2]The largest of the two studies was at unclear risk of bias for randomisation and allocation concealment, and high risk for attrition. the other was at low risk of bias for randomisation and allocation concealment, but unclear risk for attrition. Downgraded by one level for risk of bias.
[3]Small sample size and low event rate. Downgraded once for imprecision.
[4]Sensitivity analysis restricted to the only two studies at low risk of bias in key domains indicated a lack of evidence for an effect, whereas the overall analysis of all eight studies showed a positive effect. Downgraded by one level for risk of bias.
[5]Only one of the five studies was at low risk of bias, so sensitivity analysis was not possible. Downgraded by one level for risk of bias.
[6]There was moderate heterogeneity (I^2 = 48%); the second largest study showed a null result, whereas the largest and third largest showed a beneficial effect. Subgroup analysis by length of follow-up did not explain this. Downgraded by one level for inconsistency.
[7]Only one of the five studies was at low risk of bias, downgraded by one level for risk of bias.

[8]Confidence interval includes a benefit but also the null. Doesn't include potential harm. Downgraded by one level.
[9]Only two small studies reported this outcome. Downgraded once for imprecision.
[10]Both studies were at low risk of bias for randomisation and allocation concealment, but quality of life was self-reported, and this was an unblinded study. Unbalanced percentage of responders in Bernocchi 2017 (80% intervention, 63% control). Downgraded by two levels for risk of bias.
[11]Very small number of participants. Downgraded by one level for imprecision.
[12]Only reported by one small study. Downgraded by one level for imprecision.
[13]The only study reporting this outcome took place in a geriatric day hospital, which is not representative of the majority of multidisciplinary interventions. Downgraded once for indirectness.

BACKGROUND

Description of the condition

Worldwide approximately 26 million adults are living with heart failure (Bui 2011; Savarese 2017), and the condition is increasingly common in both economically developed and economically developing countries (Ponikowski 2014; Roger 2012). The crude prevalence of heart failure is typically around one to two per cent in the general population (Lloyd-Jones 2010; Ponikowski 2014). Both the incidence and prevalence of heart failure increase with age, with data from the USA indicating that the incidence of heart failure approaches 21 per 1000 population for those aged 65 and over (Benjamin 2017). The American Heart Association estimates that the heart failure incidence rate doubles for each 10-year increase in age from 65 to 85 years of age for men (Benjamin 2017; Karmali 2014), and triples for women between the ages of 65 to 74 and 75 to 84 (Benjamin 2017; Lackland 2012).

Most people with heart failure are elderly. In the English and Welsh National Heart failure audit the median age of patients discharged from hospital with a diagnosis of heart failure was 80 years - with 66% aged over 75 years and 30% aged over 85 years (NICOR 2013). With an aging population, an increasing number of people will be at risk of heart failure. In the UK, for example, Conrad 2018 reported that a decline in age- and sex-standardised heart failure incidence was seen between 2002 and 2014, but, due to the increase in size and age of the population, the estimated number of prevalent cases increased by 23%, from 750,127 in 2002 to 920,616 in 2014.

Despite the fact that in many countries survival has improved in recent years, the condition carries a substantial risk of death worldwide: 17% to 45% of people admitted to hospital die within one year (Ponikowski 2014). In high-income countries, chronic heart failure accounts for more than 10% of deaths (Kaur 2017). For low- and middle-income countries, the proportion is substantially higher, with 28% of deaths being due to chronic heart failure Kaur 2017. In addition to the risk of death, the condition has a profound impact on patients' quality of life (Bekelman 2007; Juenger 2002; Stewart 1989).

A primary diagnosis of heart failure accounts for one to two per cent of all admissions in economically developed countries and for one to three per cent of all healthcare expenditure in Europe, North America, and Latin America (Ponikowski 2014). The total annual cost of heart failure to the UK National Health Service is around GBP one billion (2% of the total NHS budget), and most of this cost (approximately 70%), is incurred by hospital admissions (Lancet 2011; NICE 2012). The estimated cost of treating heart failure was USD 30.7 billion in the USA in 2012, expected to rise to USD 69.7 billion by 2030 (Benjamin 2017).

Description of the intervention

Drug therapy is the mainstay of treatment for heart failure, although invasive procedures and devices are indicated for some patients, and patients are usually managed with a combination of medications and lifestyle advice (NICE 2010). The management of people with heart failure has evolved from a traditional model, with its emphasis on crisis intervention, towards much more proactive, preventative disease management models. These care models offer 'aggressive care' in hospital, home or clinic (Riegel 2001).

Riegel proposed three types of heart failure disease management models (Riegel 2001), and we have used her typology to identify appropriate types of intervention to include in this review.

- Case management, defined as "the active management of high-risk people with complex needs, with case managers (usually nurses) taking responsibility for caseloads working in an integrated care system" (DoH 2004)
- Clinical interventions such as enhanced or novel service provision (for example the introduction of a specialist nurse led heart failure clinic)
- Multidisciplinary interventions such as disease management interventions, defined as "a system of coordinated healthcare interventions and communications for populations with long-term conditions in which patient self-care is significant" (Royal College of Physicians 2004)

In addition to different settings such "clinical service interventions" may differ in their components, duration, intensity and the number and type of healthcare professionals involved.

How the intervention might work

Early hospital readmission in people with heart failure is extremely common. In the USA almost 30% of patients are re-hospitalised within 90 days of discharge (Gheorghiade 2013). In the EuroHeart Failure survey, which included 24 countries, 24% of people admitted with confirmed or suspected heart failure were readmitted to hospital within 12 weeks - heart failure was the principal cause of readmission (20% of readmissions), and contributed to a further 16% of readmissions (Cleland 2003). More recently, Toback 2017 reports that 17% to 27% of people hospitalised with heart failure will be readmitted within 30 days of discharge (Ghosh 2016; Jencks 2009).

Disease management interventions might reduce the risk of readmission to hospital by providing ongoing, direct support to patients post-discharge. Facilitating earlier contact with specialists and improving symptom monitoring could help manage patients in their own homes and avoid the need for frequent emergency hospital readmissions.

Why it is important to do this review

The ESC 2016 guidelines (ESC 2016), recommend multidisciplinary care, but state that there is no evidence that non-pharmacological, non-device or surgical interventions on their own improve mortality, morbidity or quality of life. The current review therefore provides a useful overview of the impact of such disease management programmes on patients' quality of life, risk of hospital readmission, and risk of mortality. We have also attempted to include data on cost-effectiveness and costs, where this information is available for the included studies.

Since the previous update of the review, there have been a number of new studies published in this area. There are now RCT data from a broader range of countries and populations than were available for the Takeda 2012 update, and inclusion of this should widen the generalisability of findings.

OBJECTIVES

To compare the effects of different disease management interventions for heart failure (which are not purely educational in

focus), with usual care, in terms of death, hospital readmissions, quality of life and cost-related outcomes.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials (RCTs) with a minimum of six months' follow-up in the review. Both individually randomised and cluster-randomised trials were eligible for inclusion. Cross-over trials could be feasible in this area, so would be included if any were identified. However, we did not identify any. Studies reported as full text, those only published as abstracts, and unpublished data were all eligible for inclusion.

Types of participants

This review focused on adults aged 18 years and over, who had been admitted at least once to secondary care with a diagnosis of heart failure. We focused on people who had been hospitalised for heart failure, because they represented a group at high risk of frequent readmission. We excluded studies dealing principally with people with cardiac disorders other than heart failure, or with heart failure arising from congenital heart disease, or valvular heart disease, or both. Where a study in the last updated review (Takeda 2012) included only a subgroup of relevant participants, we included the study if the majority of participants met the inclusion criteria. For studies identified in the most recent update, we contacted authors to source data for the relevant subgroup. Where this was not possible, we included the study if the majority of participants were eligible.

Types of interventions

We included clinical service disease management interventions (defined as inpatient, outpatient or community-based interventions or packages of care), directed specifically at people with heart failure. This excluded the simple prescription or administration of a pharmaceutical agent(s) to people with heart failure. Interventions could include or exclude patients' relatives or carers.

We used the typology of Riegel 2001 to classify studies for this review, as described in the Background section: case management, clinic-based interventions, and multidisciplinary interventions.

We did not include the following types of interventions in this review.

- Interventions that were purely educational in focus, without any follow-up phone calls or interaction between the patients and provider.
- Interventions that only consisted of exercise programmes.
- Interventions described as cardiac rehabilitation programmes, unless they also had case management elements. Cardiac rehabilitation was defined as a structured programme offered to individuals after a cardiac event to aid recovery and prevent further cardiac illness. Cardiac rehabilitation programmes typically achieve this through exercise, education, behaviour change, counselling and support, and strategies that are aimed at targeting traditional risk factors for cardiovascular disease (Taylor 2010).
- 'Generic' interventions, not exclusively aimed at people with heart failure, directed at reducing readmission or morbidity in populations of older people with a variety of long-term conditions.
- Solely telemedicine interventions, where telemedicine is defined as the “transfer of physiological data via digital cable e.g. electrocardiograph (ECG), blood pressure (BP), weight, pulse oximetry (SPO2), respiratory rate and medicine administration)”, as these were the focus of another Cochrane Review (Inglis 2015).
- Interventions that only consisted of structured telephone or videoconferencing support, including computer-assisted education and monitoring, as these were in another systematic review (Clark 2007).

We did not exclude interventions that included structured or unstructured telephone or videoconferencing support alongside other non-telemedicine components, such as attendance at a clinic or home visiting.

The comparator of interest is 'usual care', and we acknowledge that variation in local practice could introduce heterogeneity to the review. We collected data on how usual care was described in the published reports, as a source of information to explore this possibility.

We have conducted three comparisons for this review:

- case management interventions versus usual care
- clinic-based interventions versus usual care
- multidisciplinary interventions versus usual care

We have provided a narrative summary to describe separately any studies that we could not classify as one of these three types of intervention.

Types of outcome measures

We extracted outcomes for the longest available follow-up. Reporting of one of these outcomes was not an inclusion criterion for the review. We included mortality due to heart failure as well as all-cause mortality in an attempt to identify the impact of heart failure-specific interventions, which may be masked by deaths from other causes if the emphasis is on all-cause mortality (Sasieni 2017).

Primary outcomes

- Mortality due to heart failure (where this is reported separately from all cardiac causes)
- All-cause mortality
- Readmissions due to heart failure (where this is reported separately from all cardiac related readmissions)
- All-cause readmissions
- Adverse effects

Secondary outcomes

- Health-related quality of life, using a validated instrument
- Costs or cost-effectiveness

Where studies reported multiple quality-of-life assessments, we have prioritised the Minnesota Living with Heart Failure

Questionnaire (MLHFQ), as this was the most widely reported instrument.

Search methods for identification of studies

Electronic searches

We searched the following databases for this update on 9 January 2018 (search strategies in Appendix 1):

- Cochrane Central Register of Controlled Trials (CENTRAL; 2018, issue 1) in the Cochrane Register of Studies;
- Epub Ahead of Print, In-Process & Other Non-Indexed Citations, MEDLINE Daily and MEDLINE (Ovid, 1946 to 9 January 2018);
- Embase (Ovid, 1980 to 2018 Week 02);
- CINAHL Plus with Full Text (EBSCO, 1937 to 9 January 2018);
- DARE Issue 2 of 4, 2015 (Cochrane Library) – no longer updated.

The RCT filter for MEDLINE is the Cochrane Highly Sensitive Search Strategy for identifying trials in MEDLINE: sensitivity-maximising version, and for Embase, we applied terms as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011). We applied no language restrictions.

We also searched two clinical trials registries on 4 July 2018 (search terms in Appendix 1):

- ClinicalTrials.gov (www.clinicaltrials.gov);
- WHO International Clinical Trial Registry Platform (ICTRP, apps.who.int/trialsearch/).

We did not search some previously searched databases for this update, as limited resources meant we had to restrict searches to the major databases.

Details of the searches for the previous versions of the review can be found in the respective publications (Takeda 2012; Taylor 2005).

Searching other resources

In addition, we screened lists of included studies from relevant systematic reviews. We contacted study authors to clarify reported information or to obtain unpublished data.

Data collection and analysis

Selection of studies

Two review authors independently assessed the title and abstract of each reference (AT, ST or NM for this 2018 update). Two authors independently assessed the full texts of all potentially eligible papers retrieved (AT, ST or NM for this 2018 update) and coded them as 'retrieve' or 'exclude'. For non-English language papers, which appeared to be eligible for inclusion on the basis of the title and abstract, we sought the assistance of people with appropriate language skills via Cochrane TaskExchange (taskexchange.cochrane.org/). We resolved any disagreements about eligibility by discussion between at least two authors (AT, NM), with a third author (ST) being consulted where we could not reach consensus. For studies with multiple publications, we collated these so that each study rather than each report was the unit of interest in the review. We recorded the selection process in detail and described it in a PRISMA flow diagram (Liberati 2009; Figure 1).

Figure 1. Study flow diagram for 2018 update

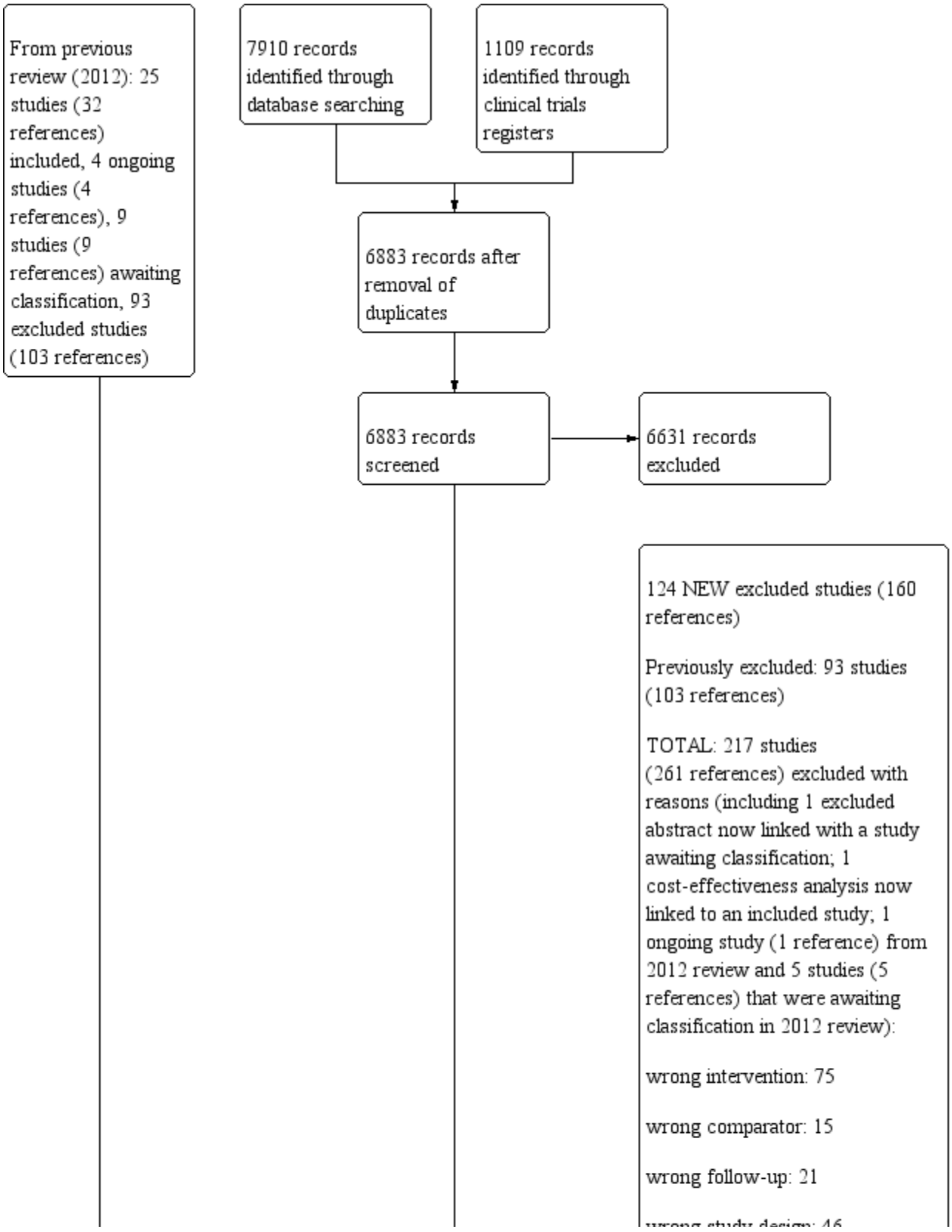
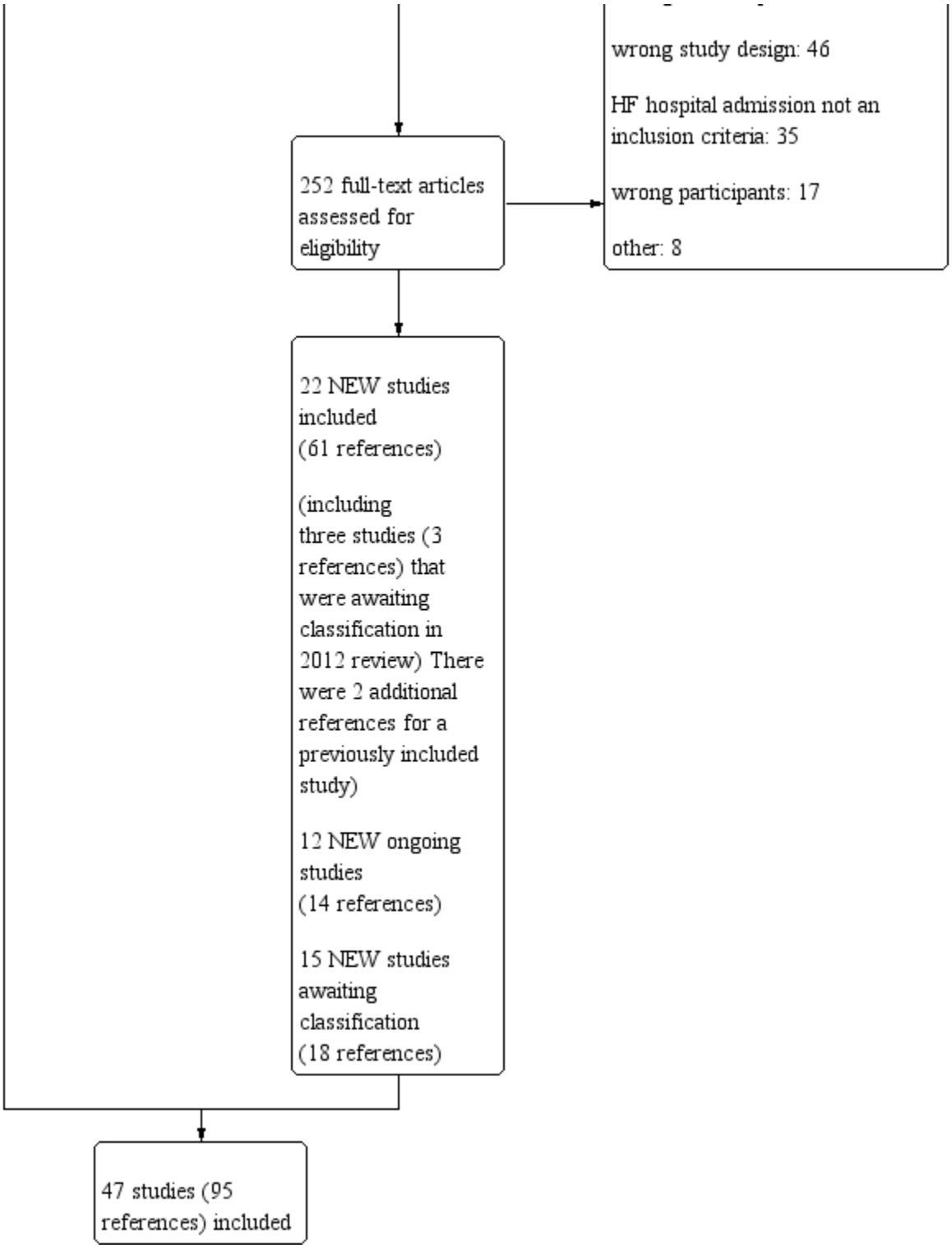


Figure 1. (Continued)



Data extraction and management

We developed a new data extraction form for this update, piloted by two review authors (NM, AT). Three review authors (AT, NM, ST), conducted the data extraction for studies published since the 2012 publication. One review author extracted study characteristics and a second author checked them, and two review authors independently extracted outcomes. An exception to this was Salehitali 2009, where a volunteer (FS), with Persian language skills, kindly carried out data extraction and assessed risk of bias. This could only be compared against the English language abstract by a second review author.

Where we were unclear about issues arising from their published papers we attempted to contact the study authors for clarification.

We extracted the following information from included studies.

- Methods: study design, total duration of study, number of study centres and location, study setting and date of recruitment
- Participants: number randomised, number lost to follow-up or withdrawn, number analysed, mean age, age range, gender, severity of condition, diagnostic criteria, comorbidities, inclusion criteria, and exclusion criteria
- Interventions: intervention, comparison
- Outcomes: primary and secondary outcomes specified and collected, and time points reported
- Notes: study funding, and notable conflicts of interest of study authors

For this update, one review author (AT), transferred data into the Review Manager 5 (RevMan 5) file (Review Manager 2014). A second review author (NM), double-checked that data had been entered correctly by comparing the data presented in the systematic review with the trial reports.

Assessment of risk of bias in included studies

Two of three review authors (AT, ST, NM), assessed all new and previously included studies by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017). We resolved any disagreements by discussion or by involving a third review author. We assessed the risk of bias according to the following domains:

- random sequence generation
- allocation concealment
- blinding of participants and personnel
- blinding of outcome assessment (assessed separately for objective and subjective outcomes)
- incomplete outcome data
- selective outcome reporting
- other bias

We graded each potential source of bias as high, low or unclear and provided a quote from the study report together with a justification for our judgment in the 'Risk of bias' table.

Categorising the interventions

We used Riegel's heart failure disease management models (Riegel 2001), to group the different interventions for synthesis as follows.

Case management models

Case management models consist of intense monitoring of patients following discharge from hospital, this is usually done by a nurse and typically involves home visits or telephone calls, or both.

Clinic-based intervention models

Clinic-based intervention models involve outpatient clinics for heart failure. They are usually run by cardiologists with a special interest in heart failure or by specialist nurses using agreed protocols to manage medication.

Multidisciplinary models

Multidisciplinary models offer a holistic approach to the individuals' medical, psychosocial, behavioural and financial circumstances and typically involve several different professions working in collaboration. The gap between hospitalisation, other healthcare delivery systems (e.g. skilled nursing facilities, hospice), and home is bridged by a team of individuals knowledgeable about heart failure and committed to patient care.

Measures of treatment effect

We analysed dichotomous data as risk ratios (RR) with 95% confidence intervals (CI) and continuous data as mean differences (MD) with 95% CIs. For quality of life, we prioritised the widely reported Minnesota Living with Heart Failure Questionnaire (MLHFQ). On this scale, a lower score indicates a better quality of life. We considered a change of five points to represent a clinically meaningful difference (Rector 1995). For outcomes where a pooled RR was calculated, we calculated the number needed to treat for an additional beneficial/harmful outcome (NNTB/NNTH), following methods outlined in the *Cochane Handbook for Systematic Reviews of Interventions* (Schünemann 2017) and using the online calculator NNT Online. We used the assumed risk with control from the 'Summary of findings' table as the 'assumed comparator risk'. Where the RR was greater than one, the CI for the NNTB includes a NNTH and a NNTB, due to inclusion of the null. For example, a NNTB of 15 could have a CI spanning from a NNTB of 8 to a NNTH of 223.

Unit of analysis issues

One study (Jaarsma 2008), had two intervention arms and a single control arm. Since the interventions were of different types (one case management and one clinic-based intervention), we treated these as separate comparisons, and as such, they never appear together in the same meta-analysis. We have therefore used the whole control arm for both comparisons. Had the two intervention arms of this study appeared within the same meta-analysis, we would have halved the control arm and used half for each comparison, to avoid double counting. For trials that reported at multiple time points, we have used the longest follow-up. We included two cluster-RCTs (Doughty 2002; Thompson 2005). Doughty 2002 randomised at the GP level, but then presented results at the participant level. Whilst this would usually present a unit of analysis problem, we accepted the study author's reasoning that the median number of participants per GP was 1.5, so the influence of clustering was small. We also carried out sensitivity analysis that excluded this study. Thompson 2005 only contributed quality-of-life data in a format that could not be pooled in the meta-analysis, so we did not re-analyse this.

Dealing with missing data

We contacted study authors to verify key study characteristics where these were unclear, for example, whether or not participants had been hospitalised for heart failure. We also attempted to obtain missing numerical outcome data from study authors where possible (e.g. when a study was identified as abstract only). Where this was not possible, we considered whether the missing data were likely to introduce serious bias. If we did not consider the data to be missing at random, we planned to explore the impact of including such studies using sensitivity analysis for primary outcomes. Since the only outcome with considerable attrition was quality of life (a secondary outcome), this was not required. We used the RevMan 5

Calculator to calculate missing standard deviations from P values where required, and noted this in footnotes to the forest plots (Review Manager 2014). We have not made any assumptions about missing data, so if study authors only reported available case data, for example for quality of life, we have used the number of responders as the denominator, not the number of people randomised.

Assessment of heterogeneity

We anticipated a high degree of heterogeneity due to differences in interventions, usual care definitions, and participant groups. We visually inspected forest plots to see if directions of effect differed between studies, and to assess the degree of overlap between studies. We calculated the I^2 statistic (Higgins 2003) to formally measure heterogeneity, using the following guide from the Cochrane Handbook for Systematic Reviews of Interventions (Deeks 2017):

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

In all cases, we considered the magnitude and direction of effects and the strength of evidence according to the P value from the Chi^2 test when interpreting the I^2 value. In particular, we considered the substantial uncertainty associated with its value when there were only a small number of studies in the meta-analysis (Higgins 2017).

Assessment of reporting biases

For outcomes reported by at least 10 trials, we constructed funnel plots to assess possible publication bias (Sterne 2017).

Data synthesis

We analysed the data using Cochrane Review Manager software, RevMan 5.3 (Review Manager 2014). Where possible and appropriate, we combined the trial results statistically using meta-analytic methods. Given the high degree of heterogeneity expected in the studies due to differences in interventions, usual care definitions, and participant groups, we applied a random-effects model for the meta-analyses. We used the Mantel-Haenszel method to pool risk ratios, and the inverse variance method to combine studies reporting health-related quality of life (to allow inclusion of a study that only reported the mean difference between treatment arms but not the group-specific data).

GRADE and 'Summary of findings' tables

We created three 'Summary of findings' tables, one for each disease management intervention (case management, clinic-based interventions and multidisciplinary interventions). We used methods and recommendations described in Section 8.5 (Higgins 2017) and Chapter 12 (Schünemann 2017) of the *Cochrane Handbook for Systematic Reviews of Interventions*, and used GRADEpro GDT software to generate the tables (GRADEpro GDT 2015).

Each table includes all five primary outcomes and the two secondary outcomes. Two review authors (AT, NM) used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to independently assess the quality of the body of evidence relating to the studies that contributed data to the meta-analyses for each outcome. Where there were studies that reported the outcomes in a way that we could not meta-analyse, we added a narrative description to the table. We describe justifications for downgrading decisions in footnotes to the table and in the section Quality of the evidence .

Subgroup analysis and investigation of heterogeneity

We carried out subgroup analysis by length of follow-up (comparing studies with six months' or less follow-up against those with over six months' follow-up). We also assessed the impact of delivery of the intervention using subgroup analysis by particular professional groups (for example pharmacists, specialist nurses).

For primary outcomes with at least 10 studies we undertook a random-effects meta-regression using the 'metareg' command in Stata, weighting studies by the standard error (SE) of the log RR, to assess whether particular intervention components were more strongly associated with positive outcomes. We only undertook meta-regression for case management studies, due to a lack of sufficient trial numbers for the other categories of intervention.

Sensitivity analysis

We undertook two sensitivity analyses, for the primary outcomes only.

- To explore the impact of the cluster-randomised control trial (Doughty 2002), by comparing the results with and without this study, for the only outcome that included this trial (clinic-based intervention versus usual care, all-cause mortality).
- To restrict the analyses to only those studies at low risk of bias in the key domains of random sequence generation and allocation concealment, and at low or unclear risk for incomplete outcome data (attrition bias). We considered blinding separately for objective and subjective outcomes separately, but since quality of life was only a secondary outcome we did not undertake sensitivity analyses for this outcome. We have therefore not included blinding as a domain for our sensitivity analysis.

We considered a sensitivity analysis exploring the impact of missing data. The most common area for missing data was in quality-of-life assessments (either missing standard deviation, which had to be imputed, or large numbers of participants missing from analyses). As this was a secondary outcome, we did not undertake sensitivity analysis for missing data.

RESULTS

Description of studies

Results of the search

Figure 1 describes the search process for this update and the previous publication. The searches for this updated review retrieved 7910 records from the databases and 1109 records from the clinical trials registries. After deduplication 6883 records remained for screening. We excluded 6631 records based on title and abstract screening and assessed 252 full-text papers for inclusion.

Based on assessment of the full texts, we excluded 160 references reporting 124 studies. We also moved a previously excluded abstract to a linked new full publication marked as 'awaiting

classification', and linked a previously excluded cost-effectiveness analysis to one of our included studies. Adding these to the previously excluded 93 studies (103 references) gives a total of 217 excluded studies (261 references).

We found 22 new studies for inclusion (61 references) and an additional two references for a previously included study. In addition to the previously included 25 studies (32 references) this gives a total of 47 included studies (95 references), with a total of 10,869 participants.

We also identified 12 new ongoing studies (14 references) and 15 new studies that are awaiting classification (18 references). For this update, we reassessed all studies previously listed as ongoing or awaiting classification, moving them either to included or excluded studies where possible.

Included studies

Control participants received 'usual' or 'routine' care in the majority of studies. In some studies, small additional components were mentioned. For example, both control and intervention participants received a programme of 'optimised' medical care after discharge from the index hospitalisation in Del Sindaco 2007, and guideline-standard management was described in Lang 2018. In two studies (Leventhal 2011; Tsuchihashi-Makaya 2013), all enrolled participants received comprehensive discharge education using an information booklet. Other studies also mentioned information sheets or short education sessions at discharge (Bekelman 2015; Bernocchi 2017; Gonzalez-Guerrero 2014). In others, a follow-up phone call or outpatient adjustment to medication was standard care (Chen 2018; Ong 2016). Dunbar 2014 mentioned an "attention control" component of telephone calls on the same schedule as the intervention participants, with information about the trial but no heart failure-specific information.

Just over half (25) of the studies were carried out at single centres, and 22 were multicentre studies. Six studies took place at two centres (Agren 2012; de Souza 2014; Kasper 2002; Kwok 2008; Lopez 2006; Thompson 2005); 13 at three to nine centres (Atienza 2004; Bekelman 2015; Berger 2010; Bernocchi 2017; Brotons 2009; DeBusk 2004; Dunbar 2014; Holland 2007; Kimmelstiel 2004; Naylor 2004; Ong 2016; Stromberg 2003; Tsuchihashi-Makaya 2013), and three at 10 or more centres (Cavusoglu 2017; Jaarsma 2008; Tsuyuki 2004).

All the studies were led by professionals from secondary or tertiary care. None of the 47 interventions were delivered in exactly the same way by the same type of personnel, although some were very similar and all the interventions had overlapping content (see Table 1). The interventions varied in site, intensity and duration (see Characteristics of included studies). Length of follow-up ranged from six months to two years.

Inclusion and exclusion criteria

The studies differed in their inclusion and exclusion criteria. All of the studies identified participants during or following an index hospital admission, or confirmed that participants had been previously hospitalised for heart failure. Participants in Gonzalez-Guerrero 2014 had acute heart failure according to European Society of Cardiology (ESC) criteria. Two studies specifically enrolled people with particular comorbid conditions; people included in Bernocchi 2017 had to have both heart failure and chronic obstructive pulmonary disease, and those in Dunbar 2014 had to have both heart failure and diabetes.

Two studies excluded people with diastolic heart failure or heart failure with preserved systolic function (Blue 2001; Tsuyuki 2004). Several of the studies mentioned excluding people with valvular heart disease requiring surgery (DeBusk 2004; Del Sindaco 2007; Doughty 2002; Holland 2007; Jaarsma 2000; Kasper 2002; Mejhert 2004; Stewart 1999a), or excluded people awaiting cardiac surgery (Atienza 2004; Holland 2007; Jaarsma 2008; Thompson 2005). Agren 2012 excluded people currently undergoing cardiac surgery, and Tsuchihashi-Makaya 2013 excluded people with end-stage heart failure. Four studies specifically excluded heart failure associated with acute myocardial infarction (Blue 2001; de Souza 2014; Ducharme 2005; Kasper 2002), and one excluded heart failure associated with cor pulmonale (Nucifora 2006). Leventhal 2011 excluded people with severe myocardial or valvular obstructive disease. The presence of serious comorbidity or other terminal illness was a common exclusion criterion, and most of the studies excluded people discharged to long-term care facilities, such as nursing homes. Clark 2015 excluded people with New York Heart Association (NYHA) class IV heart failure.

The participants enrolled in the studies

The majority of studies (36 of 47) had between 100 and 350 participants. Ong 2016 randomised 1437 people, the COACH study, reported by Jaarsma 2008, randomised 1049 and Bekelman 2015 randomised 392 people. Seven studies (Chen 2018; Clark 2015; Krumholz 2002; Lang 2018; Leventhal 2011; Rainville 1999; Shively 2013) randomised fewer than 100 participants.

For the majority of the 47 included studies, the mean or median age of participants was between approximately 67 and 80 years old. Participants in nine studies were considerably younger on average, with median or mean ages under 65 years (Capomolla 2002; Cavusoglu 2017; Chen 2018; Clark 2015; de Souza 2014; Dunbar 2014; Kasper 2002; Mao 2015; Mehralian 2014). The mean age of participants in Gonzalez-Guerrero 2014 was approximately 85 years old.

The severity of heart failure ranged across studies, with the majority (N = 37) of the studies reporting a summary statistic for participants' baseline NYHA class. The percentage of participants with moderate (class III) or severe (class IV) heart failure ranged from under one per cent in Tsuchihashi-Makaya 2013, approximately 6% in Brotons 2009 and 16% in Lopez 2006, to 75% or more in 14 of the studies (Berger 2010; Blue 2001; Chen 2018; Del Sindaco 2007; Doughty 2002; Ducharme 2005; Jaarsma 2000; Mao 2015; Ong 2016; Rainville 1999; Salehitali 2009; Stromberg 2003; Thompson 2005; Wierzchowiecki 2006). The mean (SD) NYHA class in Gonzalez-Guerrero 2014 was 2.5 (0.7) in the intervention arm and 2.3 (0.8) in the control arm. Mehralian 2014 reported that the most prevalent class was III (67.3% of the intervention group and 82% of the control group had this level of disease).

Fewer than half of the studies were carried out in Europe (N = 23). Others took place in the USA (N = 11), China (N = 3), Canada (N = 2), Australasia (N = 2), Iran (N = 2), and one each in Japan, Brazil, Taiwan and Turkey. Seven of the studies therefore took place in World Bank-defined upper middle-income countries, and the rest in high-income countries (World Bank 2018).

As would be expected in the generally elderly participants of these studies, many people had comorbid conditions. For example, of the 38 studies reporting diabetes, the proportion of people with this comorbidity ranged from 11% (Agren 2012; Leventhal 2011), to the majority (Bekelman 2015; Mao 2015), or even 100% (Dunbar 2014), as this was an inclusion criterion for that study.

Twenty-one studies were publicly funded, two by charities (Jaarsma 2000; Yu 2015a), and four by a combination of public and charity funds (Cline 1998; Leventhal 2011; Mejhert 2004; Ong 2016). A further two studies were funded by charity and industry (Jaarsma 2008; Kimmelstiel 2004), and three more by a combination of charity, public, and industry support (Holland 2007; Krumholz 2002; Tsuchihashi-Makaya 2013). Five studies were solely industry-funded (Berger 2010; Doughty 2002; Ducharme 2005; Kasper 2002; Thompson 2005), and two more were supported by both industry and public funding (Brotons 2009; Tsuyuki 2004). The remaining nine studies did not report their funding sources (Bohmer 2011; Capomolla 2002; Del Sindaco 2007; Mehralian 2014; Nucifora 2006; Rainville 1999; Shively 2013; Stewart 1999a).

Categorising the interventions

We used Riegel's classification (Riegel 2001), to group the interventions based on the content and nature of the interventions as they were described in the papers. In practice there appears to be considerable overlap between these disease management models and it was not always easy to classify them. Table 1 summarises some of the similarities and differences between the interventions. One intervention involved a day hospital, heart failure-management programme (Capomolla 2002), and was difficult to categorise. Two more did not fit into any of the classifications. Agren 2012 was an educational and psychological support intervention, and Shively 2013 was a self-management support intervention. We considered that the remaining interventions fell predominantly into the following groups:

- 28 studies and the intensive intervention arm of Jaarsma 2008 were variations on the case management approach.
- We classified seven studies as clinic-based intervention models (but with aspects of case management, i.e. telephone follow-up; Bohmer 2011); Cline 1998; Doughty 2002; Jaarsma 2008 (basic intervention arm); Mejhert 2004; Stromberg 2003; Thompson 2005)
- Nine studies had a multidisciplinary approach (Bekelman 2015; Bernocchi 2017; Cavusoglu 2017; Chen 2018; Del Sindaco 2007; Ducharme 2005; Gonzalez-Guerrero 2014; Mao 2015; Wierzchowiecki 2006). Of these, Gonzalez-Guerrero 2014 was unusual in that the intervention took place in a geriatric day care hospital, but since the intervention involved a multidisciplinary team we included it in this group.

We also attempted to classify the studies according to the key person delivering the intervention. A specialist nurse was responsible for delivering the intervention in 19 of the studies (Berger 2010; Blue 2001; Brotons 2009; Clark 2015; Cline 1998, Dunbar 2014; Jaarsma 2000, Jaarsma 2008 (basic intervention), Kasper 2002, Kimmelstiel 2004, Krumholz 2002 Lang 2018; Leventhal 2011; Naylor 2004, Nucifora 2006; Stewart 1999a, Stromberg 2003, Thompson 2005; Tsuchihashi-Makaya 2013). A pharmacist predominantly delivered the intervention in three studies (Holland 2007; Lopez 2006; Rainville 1999), and a nurse or a community nurse in 11 (Agren 2012; Aldamiz-Echevarria 2007; DeBusk 2004; de Souza 2014; Kwok 2008; Mehralian 2014; Mejhert 2004; Ong 2016; Salehitali 2009; Shively 2013; Yu 2015a). In 13 of the studies, the intervention appeared to be delivered by two or more professionals, although this did not necessarily mean they met the Riegel 2001 formal classification for multidisciplinary models, (Bekelman 2015; Bernocchi 2017; Bohmer 2011; Capomolla 2002; Cavusoglu 2017; Chen 2018; Del Sindaco 2007; Doughty 2002; Ducharme 2005; Gonzalez-Guerrero 2014; Jaarsma 2008 (intensive intervention); Mao 2015; Wierzchowiecki 2006). The intervention described by Atienza 2004 was delivered by a cardiologist, and Tsuyuki 2004 describes the research co-ordinator as being responsible for delivering the intervention.

Content of the interventions as described in the published reports.

Table 1 lists the components of the interventions as described in the published papers. Overall there appeared to be little difference in reported components between the three groups of interventions. However, it may be that the reports of the components of the different interventions were not detailed enough or systematic enough to confidently make this comparison.

Telephone follow-up

The majority (40 out of 47) of the studies in the updated review included telephone follow-up or help-line access for participants.

Education

Education delivered to participants, and in some cases, carers, appears to have been a major component in 31 of the studies included in this review. The education typically covered the diagnosis, symptoms and treatment of heart failure, and when to seek expert help.

Self-management

The majority (N = 33) of the interventions actively sought to promote better patient self-management, and participants were sometimes given heart failure diaries or notebooks to aid self-management.

Weight monitoring

Thirty of the studies mentioned daily or regular weight monitoring, or the importance of weight monitoring. Participants in these studies were often given charts or diaries in which to log their weight.

Sodium restriction or dietary advice, or both

Thirty-one of the studies mentioned participants receiving dietary advice, often from the nurse at a home visit.

Exercise recommendation

Just under half (N = 23) of the studies mentioned advice about exercise in stable heart failure or exercise promotion.

Medication review

Study reports mentioned that there was the opportunity to review participants' medications as part of the disease management programme in 25 of the studies.

Social support and psychological support

Only a minority (N = 10) of the studies specifically offered social or psychological support to participants included in the intervention.

Excluded studies

As shown in Figure 1, we excluded 217 studies in 263 references. Of these, 75 described an intervention other than a specific heart failure disease management programme, and 15 did not have 'usual care' as a comparator. We excluded a further 21 studies because they had under six months' follow-up, and 46 because they were not RCTs. heart failure hospital admission was not an inclusion criterion for 35 of the excluded studies, and 17 had the wrong participants. We excluded a further eight papers for other reasons.

Risk of bias in included studies

Our risk of bias assessments are summarised in Figure 2 and Figure 3.

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study

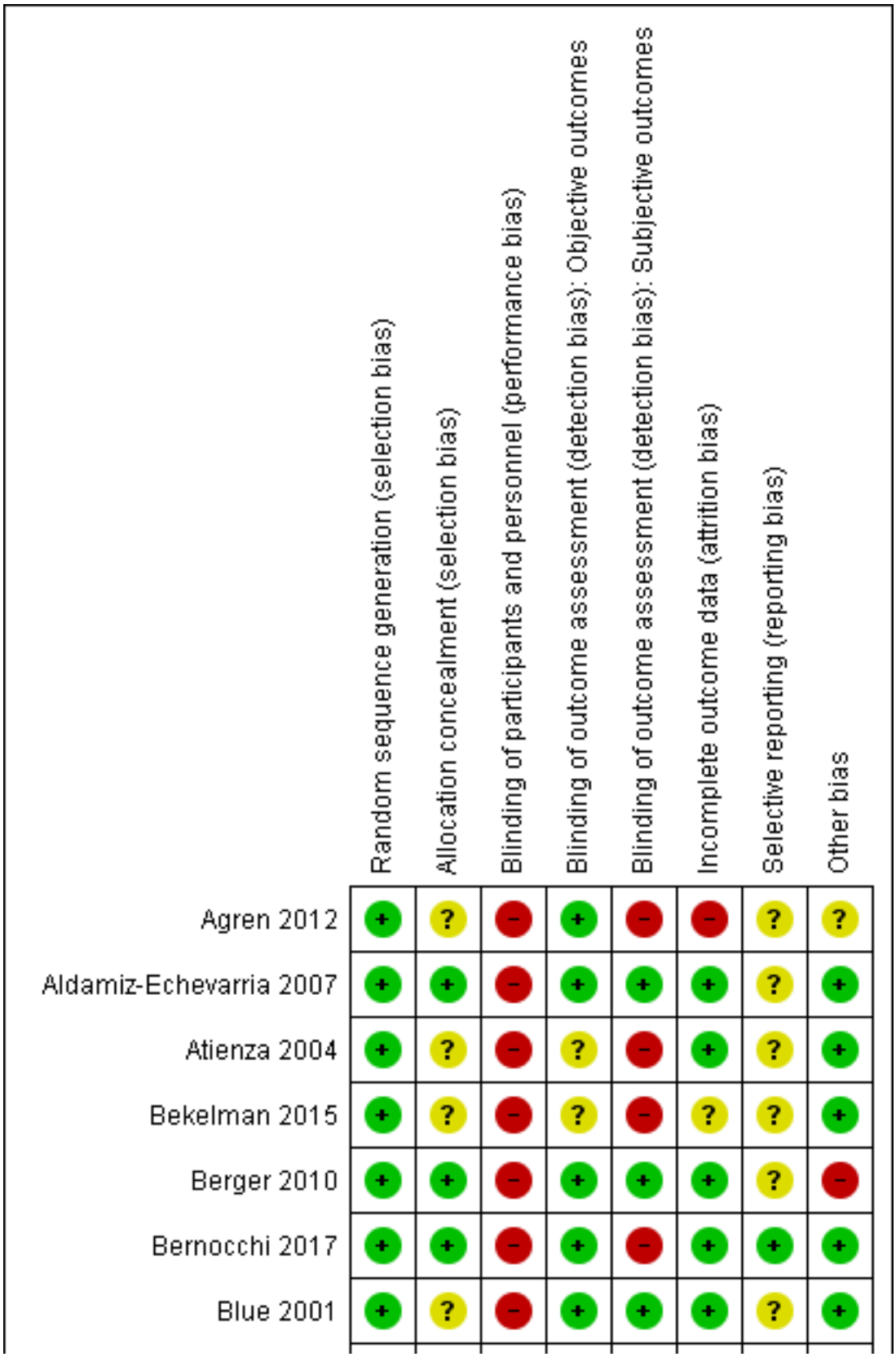
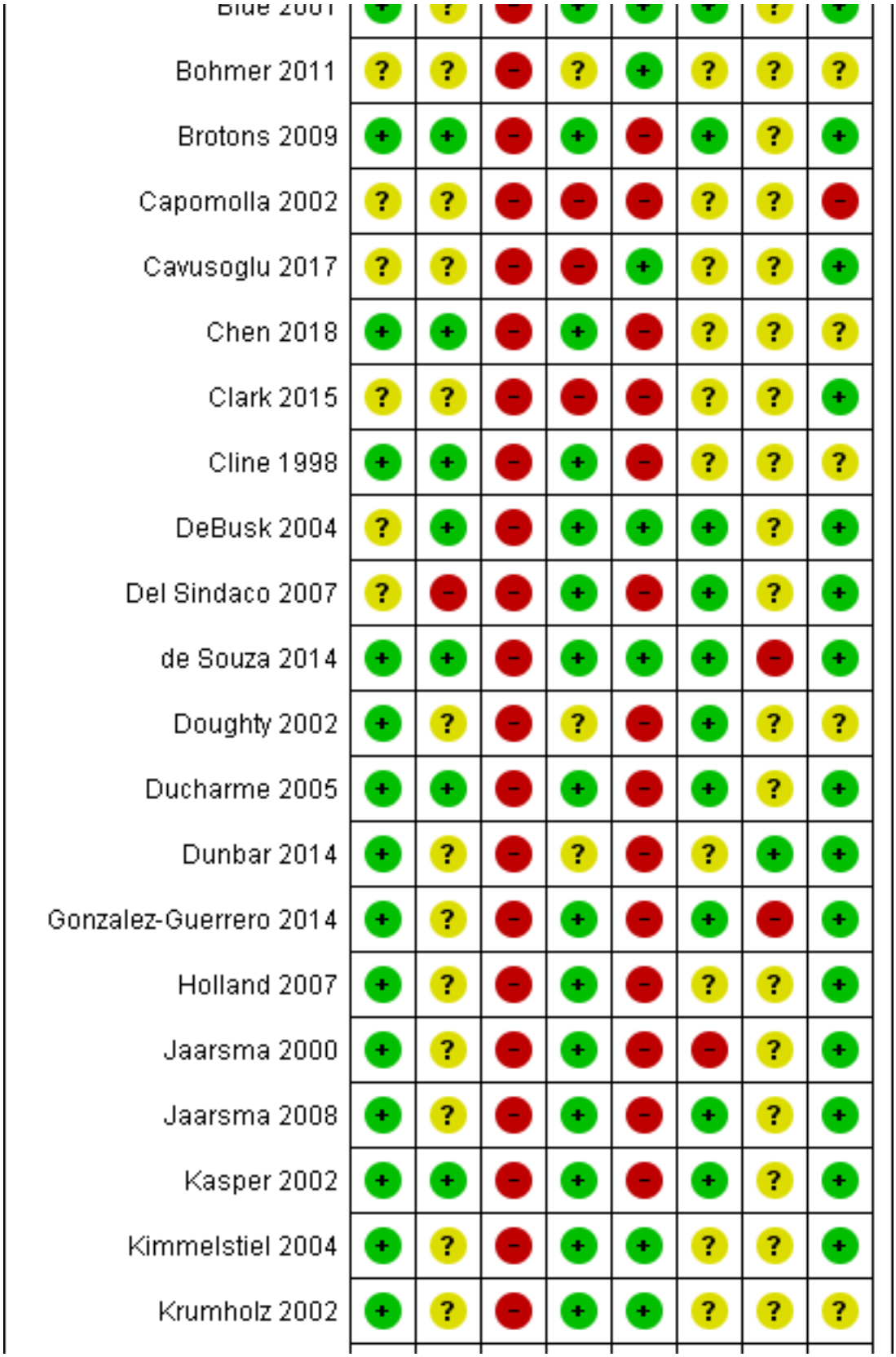


Figure 2. (Continued)



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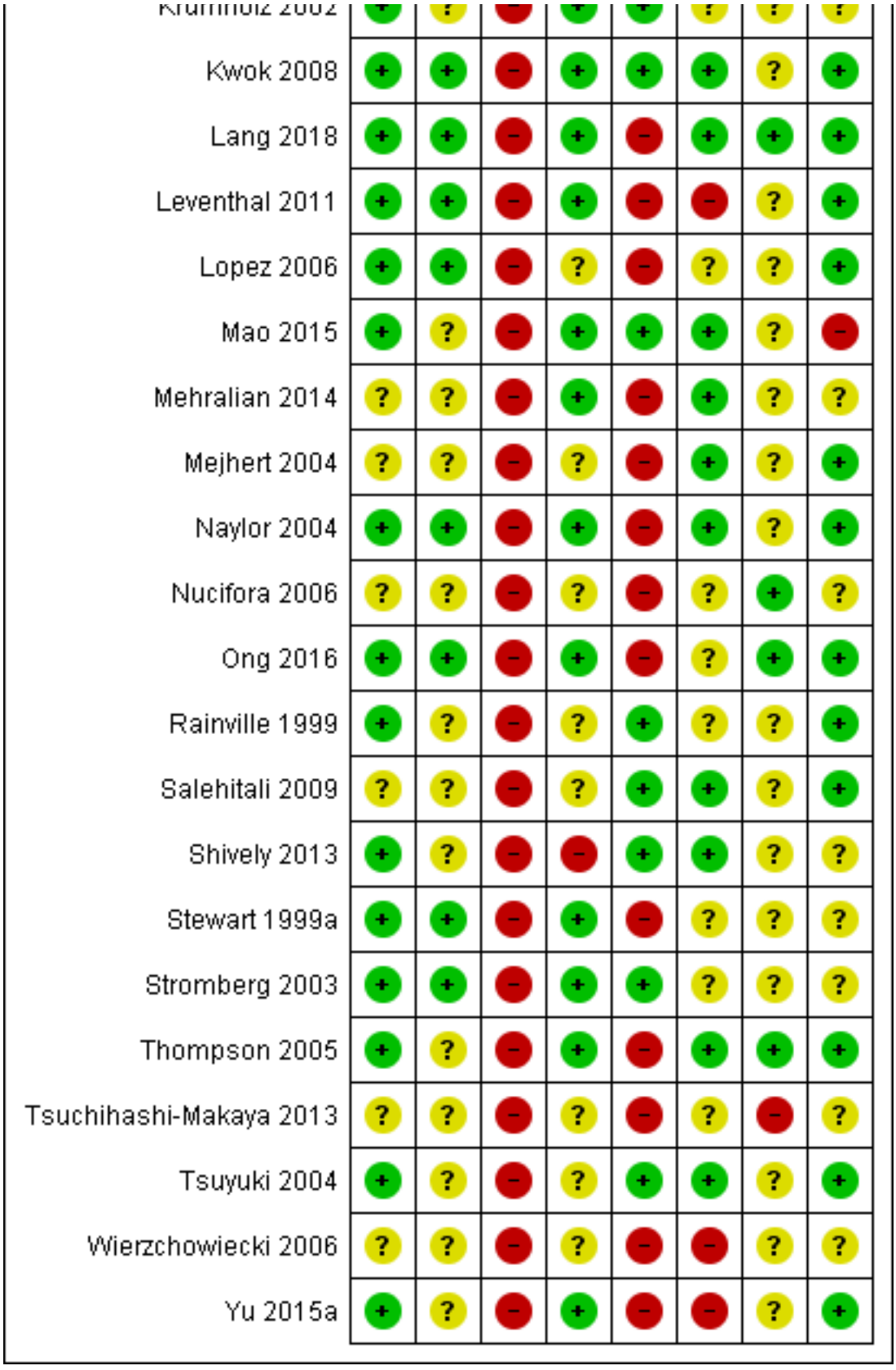
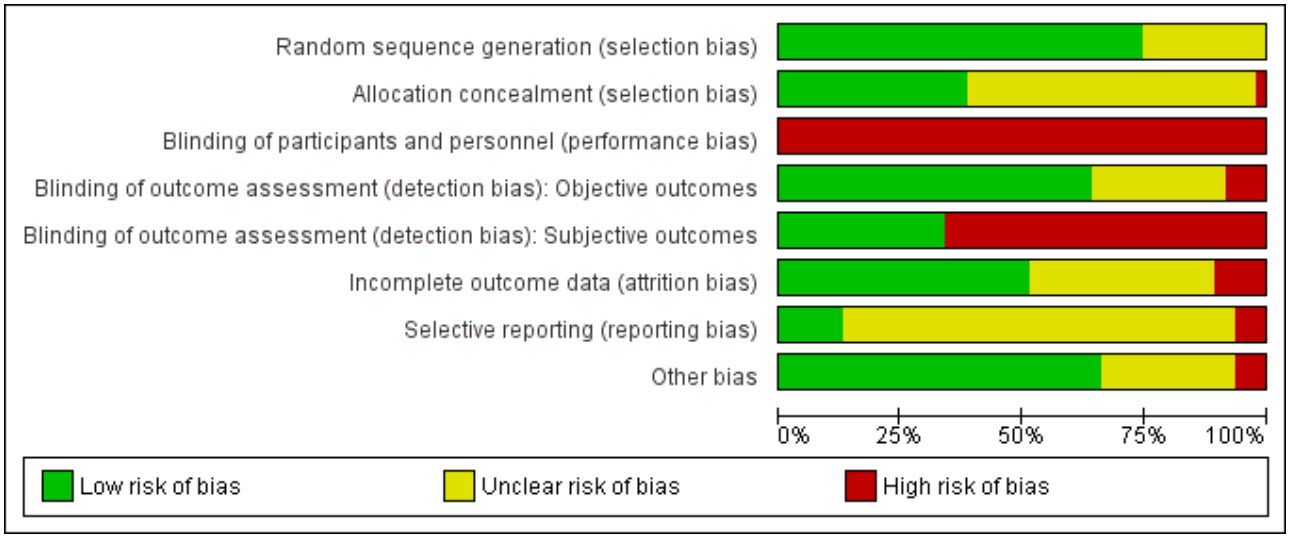


Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



Allocation

The majority of studies (N = 35) reported adequate methods of random sequence generation, and we judged them to be at low risk of bias for this domain. It was unclear if the remaining 12 studies had used appropriate randomisation methods or not, as they gave insufficient details in the publication, beyond 'randomised' (Bohmer 2011; Capomolla 2002; Cavusoglu 2017; Clark 2015; DeBusk 2004; Del Sindaco 2007; Mehralian 2014; Mejhert 2004; Nucifora 2006; Salehitali 2009; Tsuchihashi-Makaya 2013; Wierzchowiecki 2006). We did not judge any studies to be at high risk of bias for random sequence generation.

We assessed only 18 studies as having a low risk of selection bias relating to adequate allocation concealment. The majority (N = 28) did not describe this so we judged them to have an unclear risk for this domain. We assessed one study (Del Sindaco 2007), as having a high risk of bias, as eligible patients were randomised, and informed consent was then given on the basis of information relevant to the allocated study group, so selection bias is likely if people could have withheld consent if they did not like their group allocation.

Blinding

For completeness, we assessed 'blinding of participants and personnel'. However, all studies were at high risk of performance bias due to the nature of the interventions. This has an impact on the visual impact of overall risk of bias in Figure 2 and Figure 3, which perhaps detracts from the more meaningful differences between studies.

We assessed detection bias separately for objective outcomes, and the subjective, participant-reported outcome, quality of life. For objective outcomes, we assessed 30 of the studies as having a low risk of detection bias. For 13 studies, it was unclear whether or not outcome assessors were blinded to group allocation (Atienza 2004; Bekelman 2015; Bohmer 2011; Doughty 2002; Dunbar 2014; Lopez 2006; Mejhert 2004; Nucifora 2006; Rainville 1999; Salehitali 2009; Tsuchihashi-Makaya 2013; Tsuyuki 2004; Wierzchowiecki 2006). We considered four studies to be at high risk of bias for this domain (Capomolla 2002; Cavusoglu 2017; Clark 2015; Shively 2013).

We assessed the majority of studies (N = 31) as being at high risk of detection bias for subjective outcomes, since the unblinded nature of the trials meant that assessments of quality of life could be influenced by knowledge of treatment allocation. The 16 studies assessed as low risk did not report quality of life.

Incomplete outcome data

We assessed half of the studies as having a low risk of attrition bias (N = 24). It was unclear in 18 studies whether or not attrition bias was likely to affect the results. We considered five of the studies to be at high risk of attrition bias; two were particularly affected by low levels of completion for quality-of-life assessments (Agren 2012; Wierzchowiecki 2006), two had a noticeably higher attrition rate in the intervention group than in the usual-care group (Jaarsma 2000; Yu 2015a), and Leventhal 2011 was stopped early after only 42 of the required 300 participants had been recruited, so outcome data could not be collected appropriately.

Selective reporting

It was difficult to assess this domain for many of the older studies, as trial registrations were not available in many cases. We assessed the majority of studies (N = 38) as being at unclear risk of reporting bias, as we could not identify published protocols or trial registrations for these. We assessed six studies as being at low risk of reporting bias (Bernocchi 2017; Dunbar 2014; Lang 2018; Nucifora 2006; Ong 2016; Thompson 2005), since publications reported all expected outcomes. We considered de Souza 2014; Gonzalez-Guerrero 2014; Tsuchihashi-Makaya 2013 to be at high risk of reporting bias, as there were differences in outcomes listed in protocols or trials registries and those published.

Other potential sources of bias

There were no other potential sources of bias noted for 31 of the studies. We assessed the risk of other bias in 13 studies as unclear (Agren 2012; Bohmer 2011; Chen 2018; Cline 1998;

Doughty 2002; Krumholz 2002; Mehralian 2014; Nucifora 2006; Shively 2013; Stewart 1999a; Stromberg 2003; Tsuchihashi-Makaya 2013; Wierzchowiecki 2006).

We suspected a high risk of other bias for three studies. The NCT record for Berger 2010 suggested that this study had been terminated, but gave no reason for early stoppage. Participants in the intervention arm also had more severely reduced left ventricular systolic function at baseline. Not all of the intervention group in the trial by Capomolla 2002 received all the components of the intervention. Mao 2015 gave participants in the trial guideline-based medications in addition to the disease management programme, and post-hoc analyses that adjusted for this indicated that there was no evidence for the disease management programme lowering all-cause death rates once the effect of the medication had been accounted for.

Effects of interventions

See: **Summary of findings for the main comparison** Case management compared to usual care for heart failure; **Summary of findings 2** Clinic-based intervention compared to usual care for heart failure; **Summary of findings 3** Multidisciplinary disease management programmes compared to usual care for heart failure

We have presented the results of Capomolla 2002 separately because of the unique characteristics of both the intervention and the participants it was directed at (see Characteristics of included studies Table). This was a day hospital programme that offered a number of tailored therapies and specialist support (cardiovascular risk stratification, correction of risk factors for haemodynamic instability; intravenous therapy; laboratory examinations). Similarly, two other studies (Agren 2012; Shively 2013), had unusual interventions that did not fit into any of the three categories of disease management programmes, so could not be included in meta-analyses of the main interventions. Agren 2012 was an educational and psychological support intervention, and Shively 2013 was a self-management support intervention. Results of these three studies are presented under 'Other' in the section below.

Case management versus usual care

Mortality due to heart failure

None of the case management studies reported deaths due to heart failure.

All-cause mortality

Twenty-six studies reported all-cause mortality (RR 0.78, 95% CI 0.68 to 0.90; participants = 6903; studies = 26; I^2 = 30%, low-quality evidence; Analysis 1.1). The median follow-up was 12 months. Lang 2018 reported that there were no deaths in either arm, so we could not add this study to the meta-analysis. Results suggest that case management may reduce all-cause mortality. The NNTB is 25 (95% CI NNTB 17 to NNTB 54), so you could expect one death from any cause to be averted for every 25 people treated.

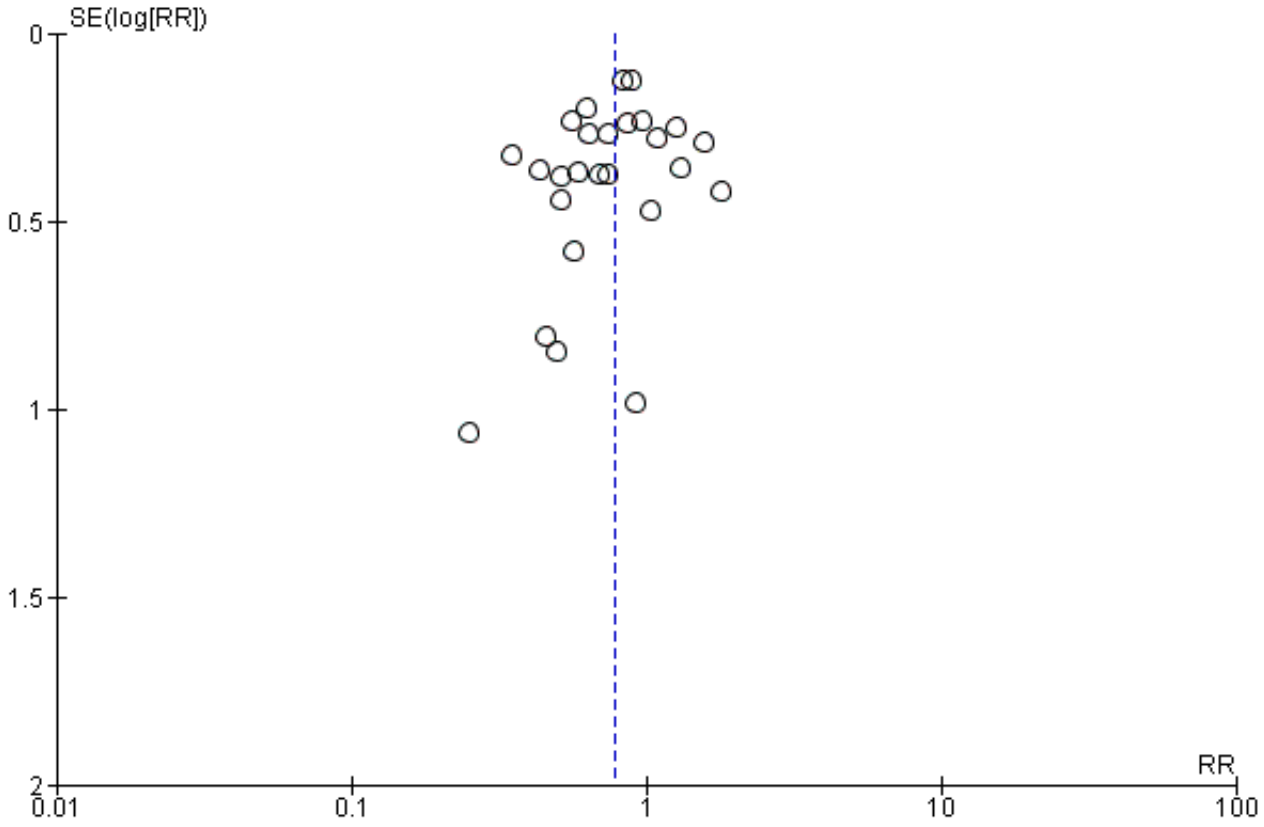
The forest plots and statistical tests did not suggest that there was important heterogeneity. Subgroup analyses by length of follow-up and by person delivering the intervention did not indicate any differences between subgroups (P = 0.22; P = 0.93, respectively).

We undertook sensitivity analysis, which limited the meta-analysis to only those studies at low risk of bias for randomisation and allocation concealment, and at low or unclear risk for incomplete outcome data (attrition bias). RR 0.67 (95% CI 0.55 to 0.82; participants = 3514; studies = 11; I^2 = 32%), indicates a stronger effect, with people receiving case management interventions having on average a 33% lower risk of all-cause mortality than people receiving usual care (Analysis 1.4).

Metaregression did not indicate that any individual intervention components were particularly associated with the success of the intervention (Table 2).

The funnel plot in Figure 4 was slightly asymmetrical, which may indicate some publication bias, so resulted in downgrading of the evidence.

Figure 4. Funnel plot of comparison 1. Case management vs usual care, outcome: 1.1 All-cause mortality - main analysis



Readmissions to secondary care due to heart failure

Twelve case management studies reported data on heart failure readmissions (RR 0.64, 95% CI 0.53 to 0.78; participants = 2528; studies = 12; I^2 = 51%, moderate-quality evidence; Analysis 1.5). The median follow-up was 12 months. Case management probably reduces heart failure readmissions, with the risk of readmission for heart failure being approximately 36% lower in people participating in a case management programme compared with those receiving usual care. The NNTB is 8 (95% CI NNTB 6 to NNTB 13), so you could expect one heart failure readmission to be averted for every eight people treated.

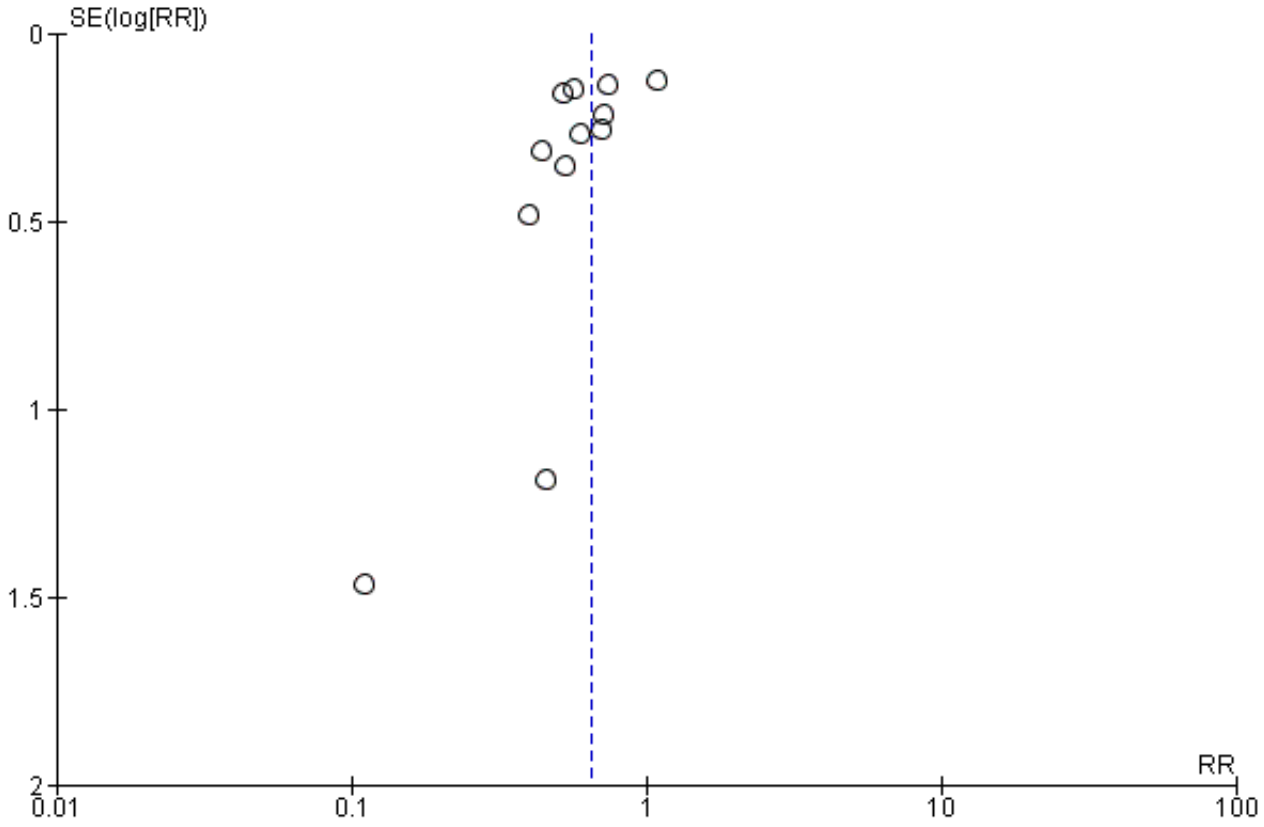
Statistical tests indicated that there may be substantial heterogeneity for this outcome. However, subgroup analysis by length of follow-up did not indicate any difference between subgroups (P = 0.33). Subgrouping by person delivering the intervention did suggest that there was a difference between groups (P = 0.002), but some subgroups contained few studies. There was strong evidence for an effect in the studies with a specialist nurse (RR 0.58, 95% CI 0.47 to 0.70). The 'other' category also showed a strong effect, notably in Atienza 2004, where the intervention was primarily delivered by a cardiologist. The subgroups of studies led by non-specialist or community nurses, or by multidisciplinary teams (within the case management framework), did not show evidence of an impact on heart failure readmissions, although there were only single studies in these groups.

Restricting the analysis of heart failure readmissions to just those studies at low risk of bias for randomisation, allocation concealment and low or unclear risk of attrition, gave a similar effect to the main analysis (RR 0.62, 95% CI 0.50 to 0.77; participants = 741; studies = 4; I^2 = 0%; Analysis 1.8).

Three studies reported data in a way that meant that we could not include them in the meta-analysis of heart failure readmissions. Kimmelstiel 2004 reported the mean (SE) number of hospitalisations for heart failure per patient-year to be 0.74 (0.10) in the intervention group and 0.73 (0.10) in the control group, RR 1.02, P = 0.93. Brotons 2009 reported the mean number of heart failure readmissions per patient to be 1.01 in the intervention arm and 1.3 in the control group. Aldamiz-Echevarria 2007 reported the total number of unplanned heart failure readmissions to be 55 and 57 in the intervention and control arms, respectively.

The funnel plot in Figure 5 is asymmetrical, suggesting possible publication bias.

Figure 5. Funnel plot of comparison 1. Case management vs usual care, outcome: 1.5 HF readmissions - main analysis



Additional Table 2 shows the results of the meta-regression. The RR for heart failure readmission in interventions with a strong education component was smaller than the RR for interventions that were not largely educational (ratio of risk ratios (RRR) 0.65, 95% CI 0.46 to 0.93; P = 0.02). This would suggest that on average, the RR for case management versus usual care in studies with a strong educational component was only 0.65 times the size of the RR for interventions without a strong educational component versus usual care. Since a lower RR indicates fewer heart failure readmissions, this would suggest that a strong educational component is an advantage.

There was some evidence from the meta-regression that a self-management component may have some slight association with a lower ratio of RR (RRR 0.72, 95% CI 0.48 to 1.07; P = 0.09), but the CI indicates that there may be no real difference. Conversely, interventions with a weight management component may actually have higher RR than those without (RRR 1.53, 95% CI 1.07, 2.18; P = 0.03). There may be other differences between studies that are not captured by the meta-regression of individual components, however, so it is important not to over-interpret these findings.

All-cause readmissions to secondary care

Fourteen case management studies reported data on all-cause readmissions in a format that we could include in the meta-analysis (RR 0.92, 95% CI 0.83 to 1.01; participants = 4539; studies = 14; I^2 = 43%, moderate-quality evidence; Analysis 1.9). The median follow-up was 10.5 months. Results suggest that case management probably slightly reduces all-cause readmissions. The NNTB is 26 (95% CI NNTH 204 to NNTB 12), so you could expect one readmission for any cause to be averted for every 26 people treated - however the CI ranges from one person potentially being harmed (i.e. one additional readmission) for every 204 treated, to one person avoiding readmission for every 12 people treated.

The I^2 result means that moderate heterogeneity may be present. Subgroup analysis by length of follow-up did not indicate any difference between studies with six months' follow-up and those with longer than six months follow-up (P = 0.19). There was evidence of a difference between subgroups of studies depending on who primarily delivered the intervention (P = 0.09). Notably, the studies where a specialist nurse delivered the intervention found that readmissions for any cause were fewer in the case management groups (RR 0.85, 95% CI 0.73 to 0.99). There was only one study where a pharmacist led the intervention, and Lopez 2006 reported lower readmissions in this intervention group (RR 0.68, 95% CI 0.45 to 1.03).

Sensitivity analysis restricting to studies at low risk of bias in key domains found similar results to the main analysis (RR 0.87, 95% CI 0.74 to 1.02; participants = 2217; studies = 6; I^2 = 42%; Analysis 1.12).

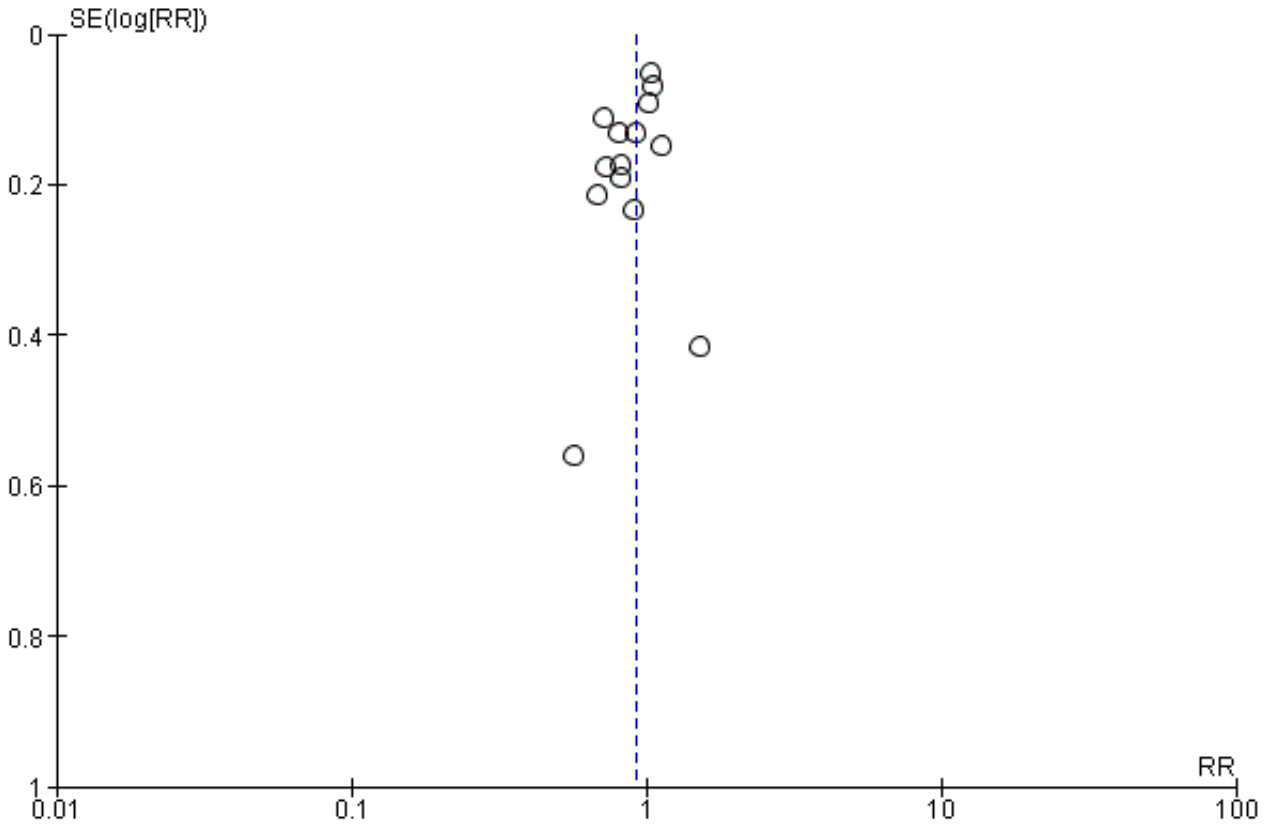
Six other studies reported data on all-cause readmissions, but not in a format that could be included in the meta-analysis. Kimmelstiel 2004 reported that the mean (SE) number of hospitalisations per patient-year was 1.48 (0.14) in the case management group and

1.40 (0.13) in the usual-care group, RR 1.05, P = 0.70. Nucifora 2006 reported that the mean (SD) readmissions per patient were 0.8 (1.2) for both arms. Aldamiz-Echevarria 2007 reported the total number of unplanned readmissions (not per patient), to be 125 and 118 in the intervention and control arms, respectively. Holland 2007 reported that 72/169 intervention participants and 70/170 control group had no emergency hospital readmissions within six months. The mean (95% CI) number of readmissions per person in Dunbar 2014 was 0.67 (0.46 to 0.87) in the intervention group and 0.95 (0.63 to 1.33) in the control group; P = 0.21. Salehitali 2009 reported a higher rate of readmissions for any cause in the control group compared with the case management group (intervention 1.65 ± 1.01, control 2.74 ± 1.07; P = 0.01).

Metaregression (Table 2) indicated that the only individual intervention component that showed any particular impact on the RR was weight management, which appeared to result in a RR of case management versus usual care that was approximately 33% higher for interventions that included this component (ratio of RR 1.32 (1.09, 1.60); P = 0.008).

The forest plot in Figure 6 is broadly symmetrical so does not suggest publication bias affects this outcome.

Figure 6. Funnel plot of comparison 1. Case management vs usual care, outcome: 1.9 All-cause readmissions - main analysis



Adverse effects

No case management studies reported adverse effects.

Health-related quality of life

Eight studies with a total of 1595 participants reported MLHFQ data in a format that could be incorporated into a meta-analysis. The median follow-up was six months. Holland 2007 only reported the mean difference between groups, not the actual data, so we used the generic inverse variance method for the meta-analysis. Where studies additionally reported another outcome (such as EQ-5D, SF-36), we did not included these results in this section to avoid double counting such studies.

Analysis 1.13 shows the eight studies on a forest plot, but due to high heterogeneity (I^2 = 76%), we have not shown the pooled effect as it is not meaningful. Subgroup analysis indicated that there may be a difference between studies reporting at six months and those with longer follow-up (P = 0.01). However, this looks to be due to the inclusion of two small studies that reported better improvement in quality of life in the usual-care group than in the case management group, both of which had the shorter period of follow-up. High attrition for this outcome led to us downgrading the GRADE rating. As our methods planned only to conduct sensitivity analysis for primary outcomes, we did not explore the impact of high attrition for this secondary outcome.

Three other studies reported using the MLHFQ tool, but did not report results in a way that could be incorporated into the meta-analysis. In a randomly selected subsample of 68 participants, Stewart 1999a reported the median (interquartile range (IQR)) change in MLHFQ at six months to be −17 (−35 to −8) in the

case management group (random sample of N = 29) and −12 (−35 to −8) in the usual-care group (random sample N = 24). Naylor 2004 reported MLHFQ scores at the end of 52 weeks, but only with reference to quartiles, and for 75 out of 117 people in the intervention group who completed a baseline assessment, and 74 out of 118 in the control group. At the end of follow-up, the quartile scores were 2.8 ± 1.8 in the case management group and 2.6 ± 1.7 in the usual-care group. In this context, a score of two indicates a first Quartile Score (435) and a score of three the second Quartile Score (418 to 35). Although Atienza 2004 reported that 220 out of 257 participants completed the MLHFQ at one year's follow-up, it was not clear how many participants there were in each group, so we could not add these data to the meta-analysis. At the end of follow-up, the mean score was 28.9 in the intervention group and 35.5 in the control group (no SD given; P = 0.01).

Four studies, which also did not report the MLHFQ, used different tools. We have not added these to the meta-analysis since the direction of effect is different and the magnitude of scores may not be comparable. Whilst it is possible to correct for this in the meta-analysis, the high degree of heterogeneity already observed means that adding further, and perhaps less compatible, studies is unlikely to be helpful, so these are summarised below.

Lopez 2006 reported very similar EuroQol (EQ-5D) scores for intervention and control group participants. By 12 months there was a small difference between the two groups, but with high SDs (64.0 (15.4) versus. 60.6 (17.8)).

Tsuchihashi-Makaya 2013 used the SF-8 tool to measure quality of life. 70 of the 79 intervention group participants and 68 of the 82 control group participants completed the questionnaire at 12 months. For the physical component score, the mean (SD) score in the intervention group was 44 (8) compared with 42 (10.5) in the control group (P = 0.36). For the SF-8 Mental component, the scores were 48 (8) and 46 (7.5) for intervention and control groups, respectively (P = 0.05).

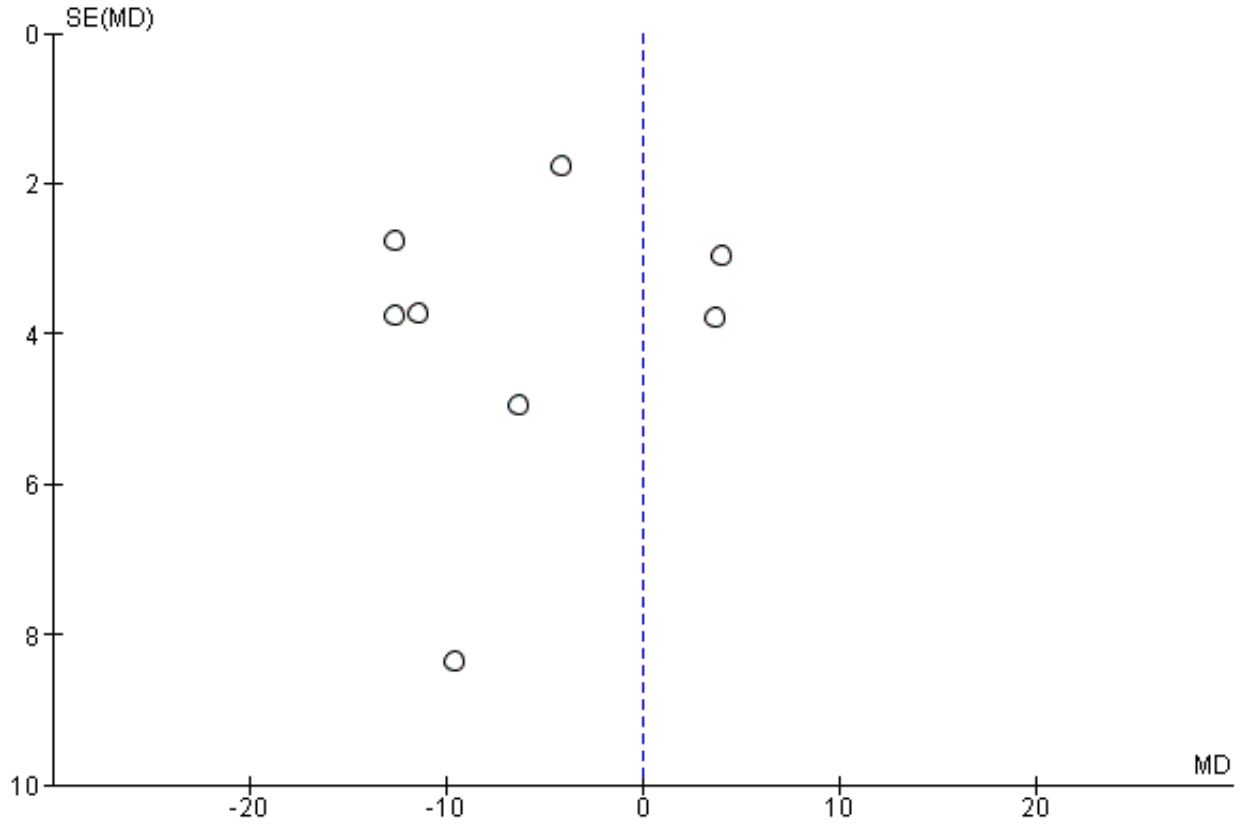
Mehralian 2014 used the Iranian version of the SF-36, and reported that the overall score was higher in the intervention group than in the control group (P < 0.05), but did not give the scores themselves. For the individual components, the role-physical domain was similar in both groups at baseline but higher in the intervention group after six months (intervention: 55.74 ± 11.65 versus control: 51.32 ± 7.51; P < 0.05). The role-emotional domain was similar at baseline and remained so at six months (58.34 ± 12.27 (intervention) versus 56.43 ± 8.67 (control); P > 0.05).

Clark 2015 used the Kansas City Cardiomyopathy Questionnaire (KCCQ). On this scale, higher scores reflect better quality of life and a five-point change in total score is a clinically important difference. In this small study, the large SDs indicate a lack of evidence for a difference between groups, either at baseline or the end of nine months' follow-up. At baseline, the intervention group's mean (SD) score was 55.38 (23.98), increasing to 62.21 (21.80) after nine months. For the control group, the mean (SD) score was 63.08 (22.90) at baseline and 60.43 (24.12) at nine months.

Jaarsma 2000, a largely educational case management intervention study, suffered severe attrition and we assessed it to be of lower quality. This study assessed quality of life for three dimensions (functional capabilities, symptoms, and psychosocial perceptions) but did not appear to use a validated tool so we have not included it here.

The funnel plot (Figure 7) is broadly symmetrical, so does not suggest publication bias affects this outcome.

Figure 7. Funnel plot of comparison 1. Case management vs usual care, outcome: 1.13 Quality of life (MLHFQ mean score at end of follow-up)



The very low-quality evidence indicated by GRADE assessment means that we are uncertain about the effect of case management on quality of life.

Cost-effectiveness

Four of the case management programmes were the subject of cost-effectiveness analyses. Ruschel (2018), reports a cost-effectiveness analysis of the de Souza 2014 study. The incremental cost-effectiveness ratio (ICER) was BRL 585 per hospital readmission visit prevented, which was favourable from the personal health services perspective, and dominant when analysed from the perspective of private healthcare. Reily (2015), reports a cost-effectiveness analysis of the Dunbar 2014 study, finding that the intervention lowered costs without sacrificing quality-adjusted life years (QALYs). The effect difference for change in QALY using the change in EQ-5D from baseline to six months was 0.04 (-0.04 to 0.11).

Two economic evaluations of the COACH study (Jaarsma 2008) were carried out. Cao (2013), stratified participants into different risk categories based on predicted 18-month mortality risk. Using a threshold value of EUR 10,000 per life-year, they found it was 83% likely that the intensive support option would be optimal for the low-risk participants, and 84% likely that the basic support option would be best for the high-risk participants. Postmus (2011), also performed an economic evaluation of the COACH study. Basic support was more cost effective than care as usual, and the ICER for intensive support was EUR 8915 per QALY. For participants with severe heart failure, cost per QALY compared with usual care was EUR 77,335 for basic support, and EUR 59,289 for intensive support.

Moertl (2013), published a cost-utility analysis of the Berger 2010 study. The incremental cost-effectiveness ratio for the case management intervention compared with usual care was EUR 3746 per QALY gained.

Various case management studies reported the costs of their programmes, although the wide range in dates of studies and different locations complicates interpretation. Lang 2018 estimated that the average cost of the REACH-HF intervention was GBP 362.61. Lopez 2006 reported that the total cost per participant was EUR 578 lower in the intervention group compared with control. The intervention's mean cost (USD 11,315) was higher than the control group's (USD 8789) in the Kasper 2002 study. Kwok 2008 reported that public healthcare and personal care costs were similar in both groups. Naylor 2004 reported mean cost savings of USD 4845 per participant for the case management intervention. Tsuyuki 2004 calculated the cost of care for all-cause events, and these were CAD 2463 lower in the patient support programme compared with usual care. Salehitali 2009 reported lower costs in the intervention group compared with the case management group (intervention: IRR 2,313,000 ± 151,490; control: IRR 2,736,800 ± 167,360).

The GRADE rating for this outcome was low, and results indicate that case management interventions may reduce costs and improve cost-effectiveness slightly, compared with usual care.

Clinic-based intervention versus usual care

We did not construct funnel plots to assess publication bias for any of the outcomes, as there were too few studies.

Mortality due to heart failure

None of the seven clinic-based intervention studies reported mortality due to heart failure as a specific outcome.

All-cause mortality

We included all seven of the clinic-based intervention studies in the meta-analysis of the effect of the intervention on mortality from any cause; the median follow-up was 12 months (RR 0.87, 95% CI 0.68 to 1.10; participants = 1686; studies = 7; I^2 = 37%, low-quality evidence; Analysis 2.1). Overall, the clinic-based intervention model may result in little to no difference in all-cause mortality. The NNTB is 29 (95% CI NNTH 37 to NNTB 12), so you could expect one death from any cause to be averted for every 29 people treated, but uncertainty associated with the wide confidence interval means you may find one extra all-cause death for every 37 people treated, or avoid one death for every 12 people treated.

Heterogeneity may not be important for this outcome according to statistical tests, but the forest plot suggests some small difference in effect. However, subgrouping by length of follow-up (Analysis 2.2), or by person delivering the intervention (Analysis 2.3), did not indicate any important differences between subgroups (P = 0.38 and P = 0.17, respectively).

Sensitivity analysis restricted to only those studies at low risk of bias for randomisation and allocation concealment, and to low or unclear risk of bias for attrition gave a different result to the main analysis (RR 0.65, 95% CI 0.23 to 1.88; participants = 296; studies = 2; I^2 = 82%; Analysis 2.4). The wide confidence intervals for this sensitivity analysis indicate a lack of evidence for effect, as there are only two small studies included.

As one of the clinic-based intervention studies was a cluster-RCT (Doughty 2002), we performed a sensitivity analysis excluding this study (Analysis 2.5). There was no substantial difference between this and the main result, although the confidence intervals and heterogeneity both increased with removal of Doughty 2002.

Readmissions to secondary care due to heart failure

Only two clinic-based intervention studies (Jaarsma 2008; Mejhert 2004), reported heart failure readmissions in a format that could be included in a meta-analysis, with a median follow-up of 18 months. Pooling the two studies indicated that there is probably little or no difference in heart failure readmissions between clinic-based interventions and usual care (RR 1.01, 95% CI 0.87 to 1.18; participants = 887; studies = 2; I^2 = 0%, moderate-quality evidence; Analysis 2.6). As the RR is over 1.0, we calculated the NNTH, and its interpretation is more complex due to the inclusion of the null. The NNTH is 290 (95% CI NNTH 17 to NNTB 23), so you could potentially expect one additional heart failure readmission for every 290 people treated; but the confidence interval goes from one person avoiding readmission for every 17 treated to one person being readmitted for every 23 treated.

Only two studies reported data for this outcome, so we did not carry out any subgroup analysis or sensitivity analysis. Doughty 2002 reported that there were 36 readmissions for heart failure in the intervention arm and 65 in the control arm, but did not report the number of participants with a readmission, so we could not pool these data.

All-cause readmissions

We pooled four studies for this outcome (RR 0.90, 95% CI 0.72 to 1.12; participants = 1129; studies = 4; I^2 = 65%, low-quality evidence; Analysis 2.9), with a median follow-up of 15 months. The low-quality evidence suggests that clinic-based interventions may result in little or no difference in all-cause readmissions. The NNTB is 19 (95% CI NNTH 16 to NNTB 7), so you could expect one readmission from any cause to be averted for every 19 people treated, but the uncertainty due to the wide confidence interval means that there could be an additional readmission for every 16 people treated, or one admission avoided for every seven people treated.

Heterogeneity was substantial for this outcome. Subgroup analysis indicated that there may be a difference between studies with six months' follow-up, and those with longer follow-up (P = 0.03; Analysis 2.10). The risk of readmission following six months of a clinic-based intervention appears to be around half that of the usual-care arm (RR 0.51, 95% CI 0.29 to 0.91). By contrast, there is no evidence that a clinic-based intervention reduces the readmission rate in the longer studies. However, the test for subgroup differences may well be underpowered given the paucity of studies and the small size of the only trial with six months' follow-up. Subgroup analysis by person delivering the intervention did not indicate any important differences between groups (P = 0.27; Analysis 2.11).

It was not possible to conduct the sensitivity analysis for this outcome as only one study (Cline 1998), was at low risk of bias for both randomisation method and allocation concealment.

Two other clinic-based intervention studies reported readmission rates in a different format. Doughty 2002 reported that the all-cause readmission rate at 12 months was 1.37 readmissions per participant per year in the intervention arm, compared with 1.84 in the usual-care group, rate difference = 0.47 per patient per year (95% CI 0.16 to 0.78). Stromberg 2003 reported total number of readmissions but not the number of participants with readmissions. The total number of readmissions was similar between groups (82 in the intervention arm and 92 in the control arm, P = 0.31). However, the mortality rate was three times higher in the control group, and once this was adjusted for in the analysis, Stromberg 2003 reported that the intervention group tended towards fewer readmissions.

Adverse effects

No clinic-based intervention model studies reported adverse effects.

Health-related quality of life

Four of the clinic-based intervention studies reported quality-of-life assessments, but it was not possible to pool these due to differences in tools used, and the way the data were reported. The median follow-up was 12 months. Doughty 2002 reported that there was no difference in MLHFQ total scores between intervention and control participants at one year. Thompson 2005 reported that the mean change in MLHFQ total score was −14.2 in the clinic-based

intervention group and −13.7 in the usual-care group, but only 46 out of 106 trial participants completed a questionnaire. Cline 1998 and Mejhert 2004 reported the Nottingham Health Profile, with mean (SD) scores of 25.3 (22.2) versus 23.4 (22.2) for clinic-based intervention and usual-care groups, respectively, in the one-year Cline 1998 study. The longer study by Mejhert 2004 reported the total mean (SD) score at 18 months to be 134 (11*) in the intervention group and 130 (125) in the usual-care group. The SD denoted by * is assumed to be a typographic error, as the total (SD) score at 12 months is 136 (107). The quality of evidence for this outcome was low, indicating that the clinic-based interventions may result in little or no difference in quality of life.

Costs

Only two clinic-based studies reported data on costs. Bohmer 2011 reported a cost saving of EUR 193.57 (EUR 1382 per person over six months).

Cline 1998 reported that the lower readmission rate in the intervention group in their study contributed to a mean reduction in overall annual costs of USD 1300 per participant (P = 0.07) over 12 months. The GRADE quality assessment was low for this outcome, indicating that clinic-based interventions may reduce costs slightly.

Multidisciplinary interventions versus usual care

We did not construct funnel plots to assess publication bias for any of the outcomes, as there were too few studies.

Mortality due to heart failure

Only two of the nine multidisciplinary intervention trials reported heart failure mortality in a way that could be included in the meta-analysis (RR 0.46, 95% CI 0.23 to 0.95; participants = 277; studies = 2; I^2 = 0%, very low-quality evidence; Analysis 3.1). The median follow-up was 12 months. The NNTB is 12 (95% CI NNTB 9 to NNTB 126), so you could expect one death due to heart failure to be averted for every 12 people treated.

There was no indication of heterogeneity. As there were only two studies, we did not carry out any subgroup or sensitivity analysis for this outcome. We are uncertain about the effect of multidisciplinary disease management programmes on heart failure mortality.

All-cause mortality

The pooled analysis for all-cause mortality (RR 0.67, 95% CI 0.54 to 0.83; participants = 1764; studies = 8; I^2 = 0%, moderate-quality evidence; Analysis 3.2), indicates that multidisciplinary teams probably reduce all-cause mortality, with people receiving this intervention having approximately 33% less risk of death from any cause than people receiving usual care. The NNTB is 17 (95% CI NNTB 12 to NNTB 32), so you could expect one death from any cause to be averted for every 17 people treated. One study not in the meta-analysis (Chen 2018), only reported composite outcomes of death or all-cause re-hospitalisations, and death or heart failure readmissions. We contacted the study author but were unable to get the data for the individual outcomes.

There was no indication of heterogeneity for this outcome and subgroup analysis by length of follow-up did not indicate any difference between groups (P = 0.37; Analysis 3.3).

Senstivity analysis restricted to only those two studies at low risk of bias for randomisation and allocation concealment, and at low or unclear risk of bias for attrition suggested a lack of evidence for any difference between multidisciplinary interventions and usual care (RR 0.65, 95% CI 0.34 to 1.25; participants = 342; studies = 2; I^2 = 0%; Analysis 3.4). However, this analysis was dominated by the Ducharme 2005 study, which carried 93.4% of the weight.

Readmissions to secondary care due to heart failure

Five studies of multidisciplinary interventions provided data that could be pooled (RR 0.68, 95% CI 0.50 to 0.92; participants = 1108; studies = 5; I^2 = 48%, low-quality evidence; Analysis 3.5).The median follow-up was 12 months. Multidisciplinary interventions may reduce the risk of readmission to hospital due to heart failure. The NNTB is 11 (95% CI NNTB 7 to NNTB 44), so you could expect one heart failure readmission to be averted for every 11 people treated.

Heterogeneity was moderate for this outcome, although subgroup analysis did not suggest any difference between six-month studies and those with longer follow-up (P = 0.13). We did not carry out the subgroup analysis by person delivering the intervention for this category, as they were all by their nature multidisciplinary. Only one study (Ducharme 2005), was at low risk of bias for randomisation and allocation concealment, so sensitivity analysis could not be carried out for this outcome.

In addition to the meta-analysis, Wierzchowiecki 2006 reported that the total number of heart failure readmissions was lower in the multidisciplinary group than in the usual-care group (13 versus 25, respectively).

All-cause readmissions to secondary care

Five multidisciplinary studies reported data on all-cause readmissions that we could pool in meta-analysis (RR 0.85, 95% CI 0.71 to 1.01; participants = 1152; studies = 5; I^2 = 40%, low-quality evidence; Analysis 3.7). The median follow-up was 12 months. Results indicate that multidisciplinary programmes may slightly reduce all-cause readmissions. The NNTB is 15 (95% CI NNTH 223 to NNTB 8), so you could expect one readmission for any cause to be averted for every 15 people treated. However, the uncertainty associated with the inclusion of the null in the RR's confidence interval means that one extra readmission for every 223 people treated and one fewer readmission for every eight people treated are also possible outcomes.

Statistical tests indicated that there may be some moderate heterogeneity, but none was detected on visual inspection of the forest plot. There was no indication that results differed by length of follow-up (P = 0.98). As with heart failure readmissions, we assessed only Ducharme 2005 as being at low risk of bias, so we could not carry out sensitivity analysis for this outcome.

Two other studies reported data in a format that could not be pooled, presenting only the total number of readmissions and not the number of people with at least one readmission. Bernocchi 2017 reported that there were 21 readmissions in the multidisciplinary group and 37 in the usual-care group. Wierzchowiecki 2006 reported fewer all-cause readmissions in the intervention group than in the control group (22 versus 35).

Adverse effects

Two multidisciplinary intervention trials mentioned adverse effects. Bekelman 2015 reported that there were no adverse effects in either study arm during the 12-month follow-up, and Bernocchi 2017 noted that, "no major side effects were recorded" during the six months of the study. We assessed the evidence as being of moderate quality using GRADE, suggesting that there may be little or no difference in adverse effects between multidisciplinary interventions and usual care.

Health-related quality of life

Due to differences in reporting, only two multidisciplinary studies could be pooled for quality of life, although four others also reported use of the MLHFQ (MD −12.21, 95% CI −16.43 to −7.99; participants = 140; studies = 2; I^2 = 0%, very low-quality evidence; Analysis 3.9). The median follow-up was 12 months. The very low GRADE rating leads to the conclusion that we are uncertain whether these interventions affect quality of life. There was no statistical evidence of heterogeneity and we could not carry out any subgroup analysis as there were too few studies. We did not carry out sensitivity analyses for this secondary outcome.

Although Wierzchowiecki 2006 also reported the MLHFQ, data were unclear and we could not include them. Del Sindaco 2007 reported that quality of life measured by the MLHFQ total score improved compared to baseline in the multidisciplinary group, but did not report data for the usual-care arm. Gonzalez-Guerrero 2014 reported the MLHFQ, but only with reference to quartile scores, where a score of two indicates a first quartile score (26 or higher), and a score of three, a second quartile score (more than 15 to 25 or less). At end of follow-up, the mean (SD) value for the intervention group was 2.7 ± 1.8, compared with 2 ± 1.8 in the control group. The median (IQR) values were 3 (1 to 4) and 2 (0 to 3), respectively (P = 0.036). Ducharme 2005 reported a “substantial improvement” in both emotional and physical quality-of-life scores of the MLHFQ for multidisciplinary care compared with usual care (P < 0.001) but did not report the actual scores.

Bekelman 2015 reported quality of life using the KCCQ. The mean (SD) change from baseline in the intervention group was 13.5 (16.7) compared with 13.5 (18.6) in the usual-care group.

Costs

Only one multidisciplinary intervention study reported costs or cost-effectiveness. In Gonzalez-Guerrero 2014, the cost per additional QALY for the disease management programme compared with usual care was EUR 38,274 from a healthcare perspective and EUR 25,390 from a societal perspective. The GRADE rating for this outcome was low, suggesting that multidisciplinary disease management programmes may be cost-effective from a societal perspective, but less so from a health-services perspective.

Other types of interventions

This section reports the results of the three studies (Agren 2012; Capomolla 2002; Shively 2013), that did not fit into one of the three categories used in this review. The 24-month data from the study by Agren 2012 were reported by Liljeroos 2015.

Mortality due to heart failure

None of the studies reported mortality due to heart failure.

All-cause mortality

The Agren 2012 long-term follow-up (Liljeroos 2015), reported that all-cause mortality was lower in the intervention group (12/71, 17%) than in the usual-care group (22/84, 26%).

Readmissions due to heart failure

After 24 months, 31 out of 71 participants (38%) of the Agren 2012 study's intervention group were readmitted for heart failure, compared with 33/84 (34%) in the control group; P = 0.64 (reported by Liljeroos 2015).

All-cause readmissions

Capomolla 2002 noted a substantial reduction in hospital readmissions in the intervention group (total number of hospital readmissions at mean 12 (SD 3) months' follow-up: 13 versus 78, P < 0.00001), but the generalisability and quality of this study are very unclear. It is also unclear if these are all-cause readmissions or readmissions for haemodynamic instability. Capomolla 2002 also reported that eight day-hospital participants and 35 usual-care participants had at least one rehospitalisation during follow-up (P < 0.05).

The number of people with at least one all-cause readmission in the long-term follow-up of the Agren 2012 study was reported by Liljeroos 2015. In the intervention group, 51 out of 71 participants (72%) were readmitted, compared with 58 out of 84 participants (68%) in the control group; P = 0.72.

Shively 2013 reported data on hospital readmissions and emergency department visits at six months' follow-up, with no statistically significant differences reported between intervention and control groups. At six months, the mean (SD) number of hospital admissions per person was 0.21 (0.41) in the intervention group and 0.32 (0.48) in the usual-care group.

Adverse effects

None of the 'other' studies reported adverse effects.

Quality of life

Capomolla 2002 reported the time trade off method for assessing quality of life. In the day-hospital group this was 0.72 (SD 0.17), meaning that participants were willing to trade 10 years of their present health for 7.2 years of excellent health. In the usual-care group, the mean (SD) was 0.63 (0.22), indicating that participants were willing to trade 6.3 years of their present health.

Agren 2012 reported quality of life using the SF-36 tool. The mental component score was very similar at end of follow-up in both groups (intervention −4.55 (11.2); control −4.22 (11.9); P = 0.88). The physical component score was also similar at 12 months (−1.9 (9.8) versus −0.5 (7.9) for intervention and control, respectively; P = 0.39).

Costs

Capomolla 2002 reported a higher QALY for the day-hospital group than the usual-care group (79.4 versus 70.5, P = 0.01). The cost/utility ratio was better for the day-hospital model, at USD 2244 compared with USD 2409 for the usual-care group. They also reported a cost saving of USD 1068 per QALY gained.

DISCUSSION

Summary of main results

This updated review contains 47 RCTs of disease management interventions. Of these, 28 RCTs were of case management interventions, seven were clinic-based interventions, and nine had a multidisciplinary approach. One of the clinic-based studies also had a case management arm. Three RCTs had interventions that we could classify into one of these groups. The 47 RCTs contained a total of 10,869 participants. We have summarised results for each main intervention category in Summary of findings for the main comparison; Summary of findings 2; and Summary of findings 3.

Mortality due to heart failure was poorly reported, with many studies only reporting cardiovascular-related mortality. There were no data for this outcome for the case management interventions, nor for clinic-based interventions. Two multidisciplinary interventions reported this outcome, but we assessed the evidence to be of very low-quality, so we are uncertain about their effect on heart failure mortality.

Mortality from any cause was reported for all three types of interventions. After taking into consideration the GRADE quality ratings, results indicated that case management interventions may reduce all-cause mortality, clinic-based intervention models appear to have little to no effect, and multidisciplinary interventions probably reduce all-cause mortality.

Heart failure readmissions to secondary care were not always distinguished from cardiovascular-related readmissions. Where studies reported this outcome separately, we found that case management interventions probably reduce heart failure readmissions. The strongest evidence was when the intervention was led by a specialist nurse. The clinic-based interventions probably made little or no difference to the risk of readmission for heart failure, and evidence suggested that the multidisciplinary programmes may reduce the risk of being readmitted to hospital for heart failure.

Case management studies probably slightly reduce readmissions to hospital for any cause. As for heart failure readmissions, evidence was strongest for those interventions delivered by a specialist nurse. Clinic-based intervention models appeared to have little to no effect on the risk of readmission for any cause, whereas multidisciplinary programmes may slightly reduce the risk of all-cause readmission.

Very few studies mentioned adverse effects. None of the case management or clinic-based intervention models reported this outcome, and two multidisciplinary intervention studies mentioned that no adverse effects were reported during the trials.

It was difficult to assess the quality-of-life outcome due to differences in reporting methods and very high attrition rates. For case management and multidisciplinary interventions, the quality of evidence was very low, so we are uncertain of the evidence for these. Evidence for clinic-based intervention models suggests that these may result in little or no difference in quality of life.

Low-quality evidence suggested that case management models may reduce costs and improve cost-effectiveness slightly, compared with usual care. Clinic-based interventions may reduce costs slightly, and multidisciplinary models may be slightly cost-effective.

Overall completeness and applicability of evidence

The review question set out to explore the evidence for disease management interventions for heart failure. We included 47 studies with a total of 10,869 participants. Just under half of the studies took place in Europe and 13 were in North America; seven were in upper-middle income countries as defined by the World Bank 2018. Mao 2015, whose study took place in Taiwan, emphasised the importance of evaluating disease management programmes in non-Western countries. The more extensive literature available for this update has therefore somewhat broadened the applicability of the evidence beyond that available at the last update (Takeda 2012).

The included studies randomised participants with a range of heart failure severity and co-morbidities. Although participants in most studies were aged on average between 67 and 80 years, 10 studies had younger participants on average, and one had very elderly participants. Some studies excluded participants with serious co-morbidities, those awaiting surgery or those who had heart failure associated with acute myocardial infarction. This may affect generalisability as people with heart failure often have multiple chronic conditions. However, the diversity of the 47 studies does appear to be broadly representative of the population of interest.

The range of interventions and countries where the studies took place mean that the comparator 'usual care' differed between them. Whilst this adds heterogeneity to the analysis of outcomes, it does to some extent reflect the 'real world' situation and widen the applicability of findings.

Complex interventions of this kind differ widely in terms of content, delivery and setting. Intervention-specific factors can therefore contribute to the success of the programme, and heterogeneity in these can affect the overall results described in this review. We explored the contribution of individual components of an intervention, but it was difficult to clarify the exact structure of each intervention due to limitations in reporting. The transferability of complex interventions is also difficult, as the interaction between components may be equally as important as the impact of each individual aspect. Undocumented aspects, such as the relationship between patients and their carers, the influence of a patient's particular domestic circumstances, and the dynamic between members of the multidisciplinary team, may also be influential.

The outcomes for this update were more narrowly focused than those for the previous update (Takeda 2012), aiming to provide more succinct patient-relevant outcomes specific to the disease and intervention in question. However, it was notable that heart failure readmissions and mortality due to heart failure were reported more rarely than general cardiac-related readmissions or causes of death. This led to a less complete summary of evidence for these outcomes. Reporting cause of death may not be particularly reliable in this frail, elderly, multimorbid population, and heart failure may be contributing to another cause of death. The beneficial effect of case management programmes in reducing all-cause mortality is, therefore, a helpful indicator of their broader impact.

Quality of the evidence

Evidence from case management interventions was moderate for heart failure readmissions, all-cause readmissions and costs. We downgraded quality for publication bias, imprecision and indirectness, respectively. The evidence for all-cause mortality was low due to high risk of bias and suspected publication bias. We assessed quality-of-life data as being very low-quality, due to risks of attrition and detection bias, inconsistency (heterogeneity), and imprecision.

The GRADE quality assessments for outcomes of clinic-based interventions were low for all outcomes except heart failure readmissions, which we assessed as having moderate-quality evidence. Low-quality assessments for all-cause mortality and all-cause readmissions were due to high risk of bias, imprecision (CI including the null). The moderate rating for heart failure readmissions was due to the only downgrade being for risk of bias. We downgraded the quality-of-life outcome by two levels due to risk of detection bias (unblinded outcome), and high attrition. We downgraded the cost outcome for indirectness, due to the age of the cost data, and for imprecision associated with the small sample size. We assessed all-cause mortality as moderate-quality evidence (downgraded once for risk of bias). We downgraded both adverse events and costs once for imprecision, so we assessed them as being of moderate quality. Our GRADE assessment for both heart failure readmissions and all-cause readmissions was low-quality, being downgraded once for risk of bias and once for inconsistency due to heterogeneity (heart failure readmissions), or for imprecision due to wide confidence intervals including the null (all-cause readmissions). The evidence for mortality due to heart failure was of very low quality, downgraded for indirectness, risk of bias and imprecision due to the low event rate. Similarly, quality-of-life evidence was very low quality, downgraded twice for risk of bias (detection and attrition) and imprecision.

Potential biases in the review process

Although we searched key databases and trials registries, it is possible that we did not identify some relevant publications. For the majority of outcomes there were too few studies for a funnel plot to be constructed, so we were not able to assess the possibility of publication bias. There were also too few studies for robust subgroup analyses for several of the outcomes. We had difficulty classifying some of the studies, so studies where the intervention was poorly described may not have been assigned to the most appropriate group, had the most appropriate person recorded as delivering the intervention, or had all the components of the intervention listed accurately. One of the key inclusion criteria for this review was the requirement for study participants to have been admitted to secondary care at least once for heart failure. This was often unclear in the publications, and we contacted many study authors for further information. The inclusion of such studies may therefore be biased towards those where study authors were responsive and able to provide the necessary information.

Agreements and disagreements with other studies or reviews

The previous update of this review (Takeda 2012) concluded that case management interventions led by specialist nurses reduce heart failure readmissions, all-cause readmissions and all-cause mortality after 12 months' follow-up. The authors of the previous update found that multidisciplinary interventions may be effective in reducing readmissions for heart failure or any cause, but found little evidence for effectiveness of clinic-based interventions. In addition to adding new studies to the review, we have used the GRADE system to assess the quality of evidence and this has affected the interpretation of results. This current update agreed with the previous review in finding that case management interventions probably reduce all-cause mortality, readmissions for heart failure, and probably slightly reduce readmissions for any cause. Our subgroup analyses also indicated that interventions led by a specialist nurse were more effective than others in reducing readmissions for either heart failure or any cause. As with the previous review, we found evidence that multidisciplinary interventions may slightly reduce the risk of readmission for heart failure or any cause. Unlike the previous update, the larger body of evidence reviewed now indicates that multidisciplinary interventions probably reduce all-cause mortality. As previously, we found little to no effect of clinic-based interventions for heart failure on any of the clinical outcomes in the review. Evidence for the effect of disease management programmes on quality of life remains very uncertain. We reviewed costs and cost-effectiveness for this update but not the previous one. We found that case management interventions probably reduce costs and improve cost-effectiveness slightly, that clinic-based interventions may reduce costs slightly, and that multidisciplinary models are probably slightly cost-effective.

The most similar recent systematic review to our own is that by Huntley 2016, who reviewed the impact of case management interventions in the community for people with heart failure, in terms of reduction in hospital admissions or readmissions. That review included 17 RCTs and five non-RCTs, and was not restricted to people who had been admitted to hospital for heart failure. The authors found that hospital-initiated case management interventions reduced readmissions, as was found in our review. They did not find much difference in costs between case management and usual care, whereas we found that such interventions probably reduce costs and improve cost-effectiveness slightly.

Oyanguren 2016 conducted a meta-analysis of management programmes for people with heart failure, which included 66 RCTs. It is important to note that these included a broader spectrum of management interventions than just disease management programmes of the type described in our own review (for example trials on use of beta-blockers), and there was also no restriction on length of follow-up. The authors did not divide the studies into case management, clinic-based intervention and multidisciplinary programmes, but found overall that heart failure management interventions reduce mortality and readmissions.

Other systematic reviews in this area include a meta-analysis and cost-effectiveness study of six 'care in the home' trials, broadly comparable with case management interventions (Fergenbaum 2015). The authors reported that care in the home reduced the number of hospitalisations (as did our review), but not all-cause mortality (unlike our review). They also reported better quality of life for people who had care in the home. However, the authors also noted that the quality of evidence indicated uncertainty over outcomes. As with our current review, they found care-in-the-home interventions to be less costly and more cost-effective than usual care.

A recent meta-analysis of 16 RCTs of multidisciplinary, heart failure clinic-based interventions (Gandhi 2017), reported lower odds of heart failure hospitalisation (but not all-cause hospitalisation), and lower odds of all-cause mortality for people attending the heart failure clinics. Differences between the conclusions of the Gandhi 2017 review and our own, less optimistic, findings, are likely due to the different studies included - we excluded nine of their studies from our own review for various reasons, including having a follow-up of under six months, having the wrong participants or comparator, and because hospital admission was not an inclusion criterion.

There is some overlap in included studies between our own review and the network meta-analysis of transitional care services published by Van Spall 2017, although that analysis included a wider range of interventions, and studies with shorter follow-up than our own. Interestingly, they found that home visits by nurses were the most effective services in terms of decreasing all-cause readmissions, followed by nurse case management. Both of these would fall into the 'case management' category in our review.

It is interesting to compare our findings with the recommendations of the 2016 ESC Guidelines (ESC 2016), which recommend the use of multidisciplinary management programmes to reduce the risk of heart failure-related hospitalisation and mortality. Our review supports the likely reduction in all-cause mortality for people treated by multidisciplinary teams, with low-quality evidence also indicating a possible reduction in heart failure readmissions. In addition, our review found that a case management approach, particularly when led by specialist nurses, can also be effective in reducing all-cause mortality and HF readmissions.

AUTHORS' CONCLUSIONS

Implications for practice

We found limited evidence for the effect of disease management programmes on mortality due to heart failure, with no case management or clinic-based interventions reporting this outcome specifically; the evidence from multidisciplinary studies was of very low quality. However, it is difficult to classify death due to heart failure in this elderly, co-morbid population. The use of all-cause mortality may therefore be a better indicator of the intervention's impact than mortality due to heart failure.

The available evidence suggests that either case management or multidisciplinary models are likely to deliver reductions in overall mortality and heart failure readmissions, and may reduce all-cause readmissions. The more limited evidence from clinic-based models generally found little or no effect on mortality or readmissions for heart failure or any cause. For case management models, the evidence suggests that a specialty trained heart failure nurse is important, a strong education component may be beneficial, but that weight monitoring may be of limited value**.**

There was a lack of evidence for adverse events, but this is not unexpected due to the nature of the interventions. It would be difficult to identify and collect specific adverse effects of disease management interventions – for example, widening gaps in access to services for people unable to receive home visits or answer telephone calls.

Despite many studies reporting quality-of-life assessments, the evidence remains of very low-quality for case management and multidisciplinary interventions, so results are uncertain for this outcome. The evidence for clinic-based interventions was of low quality, and the studies appear to make little or no difference to quality of life.

Variations in study location and time of occurrence hamper attempts to review costs and cost-effectiveness, but limited data suggest that these models are cost-effective**.**

Implications for research

Despite the inclusion of 22 new studies since the last update of this review, there remains a gap in the evidence for quality of life, as this outcome is poorly reported and suffers high attrition. For the mainly elderly, heart-failure populations in the studies included in this review, the potential to improve quality of life is an important consideration both for patients themselves, their carers and health professionals. Improved reporting of this outcome in future trials would be helpful in strengthening the evidence for this patient-relevant outcome.

The assessment of complex interventions is an active area of research, and new methods could be useful for improving interpretation of studies. For example, Freeman 2018 describes methods for undertaking a component network meta-analysis to assess the effects of specific components of complex interventions. Any such work would also require an improvement in the reporting of randomised controlled trials (RCTs), as it is often difficult to identify exactly what components have been included in an intervention and to estimate the relative time spent on each.

It is also worth considering whether a traditional meta-analysis of RCTs is the best approach for evaluating complex interventions. Mixed methods may be more helpful in analysing the many interacting components of disease management programmes, and helping to understand the various impacts on their effectiveness.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agren 2012

Methods	Multicentre RCT (2 hospitals) Recruiting: January 2005-December 2008 Follow-up: 3 and 12 months (with 24 months' long-term results in subsequent publication by Liljeroos 2015) Intervention category: other Person delivering the intervention: nurse
Participants	Country: Sweden, setting described as hospital-based, but interventions took place in participants' homes or the HF clinic depending on participant preference. Participants: N = 155: 71 (46%) in intervention group, 84 (54%) in usual-care group Mean ± SD age 69 ± 13 in intervention group, 73 ± 10 in usual-care group Male sex: 49 (69.1%) in intervention group, 68/84 (80.9%) in control group Ethnicity: NR Actual severity of HF in study participants at recruitment (NYHA class, N (%)): • intervention group, class I, N = 0; class II, N = 25 (35%); class III, N = 39 (55%); class IV N = 7(10%); • control group, class I N = 0; class II, N = 25 (30%); class III, N = 43 (51%); class IV, N = 16 (19%) Median EF%: NR Inclusion criteria: • a dyad consisting of a patient diagnosed with HF based on the ESC guidelines, NYHA functional class II-IV, with a partner living in the same household, recently discharged from hospital (i.e. 2-3 weeks) after a HF acute exacerbation Exclusion criteria: • dementia or other severe psychiatric illnesses • drug abuse • difficulties in understanding or reading the Swedish language • undergoing cardiac surgery, including cardiac transplant • participating in other studies
Interventions	Median duration of intervention: 12 weeks Intervention: • psychosocial support to maintain and strengthen physical and mental functions, knowledge, and perceived control to make participants feel involved and reduce their stress and their partners' burden. • 3 nurse-led, face-to-face counselling sessions of at least 1 h each, including education on HF with booklets and computer-based education using a CD-ROM program, and other written teaching materials • intervention focused on changing thoughts and behaviours and implementing strategies for self-care • dyads were also encouraged to talk about lifestyle changes, communication, and prospects and learning to live with lifelong HF Comparator:

Agren 2012 *(Continued)*

- dyads in the control group received care as usual, including traditional care in hospital and outpatient education and support. At present, this care is mainly focused on the participant's needs. The partner is not systematically involved in the follow-up focusing on education and psychosocial support.

Outcomes	Primary outcome: unclear Outcomes: perceived control, self-care, HRQOL, depression, caregiver burden SF-36 for self-rated health BDI-II CAS: 4 items, 2 about perceived control and 2 about helplessness EHFscBS Caregiver Burden Scale
Notes	Funding: "Funding: Grants from Linkoping University, Swedish Research Council, Swedish Institute for Health Sciences, Heart and Lung Foundation, Heart and Lung Disease National Association, and Lions Research Foundation". Disclosures: none Data source: published data only 165 dyads accepted for study participation, 10 then withdrew before baseline assessment, 155 dyads randomised after baseline assessment, 71 (46%) randomised to experimental group and received intervention, 84 (54%) randomised to control group 7 intervention participants and 9 intervention partners; 6 control participants and 9 control partners did not complete 3 months' follow-up. At 12 months, 14 intervention participants, 13 intervention partners, 21 control participants and 26 control partners did not complete follow-up. Liljeroos 2015 reports long-term follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation code was developed using a random-number table
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (performance bias)	High risk	No blinding possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "both data collectors, and researchers entering the data were blinded to group assignment"
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-completed QoL questionnaires, no blinding of participants
Incomplete outcome data (attrition bias) All outcomes	High risk	Agren 2013: 14/71 (19.7%) intervention and 21/84 (25%) control participants did not complete - not balanced

Agren 2012 *(Continued)*

		Liljeroos 2015 (long-term follow-up): low for readmissions and mortality - all randomised participants included in analysis; high for QoL data: Although missing data in the SF-36 were imputed by the means of the subscale if only 1 item in the subscale was missing, only 62% in both intervention and control groups completed questionnaires so 38% of dyads were not included.
Selective reporting (reporting bias)	Unclear risk	The study was registered at ClinicalTrials.gov, identifier: NCT02398799, after participant recruitment began. Quote: "The reason for this is that when recruitment began, it was unusual to register this type of intervention studies." However, reported outcomes are in line with the study's objectives.
Other bias	Unclear risk	There was a higher proportion of men in the intervention group than the control group (80.9% vs 69.1%)

Aldamiz-Echevarria 2007

Methods	Single-centre RCT Recruitment dates: February 2001- June 2002 Follow-up: 12 months Intervention category: case management Person delivering the intervention: nurse
Participants	Country: Spain N randomised: 279 Intervention (N = 137) vs control (N = 142) Mean (SD) age: 75.3 (11.1) vs 76.3 (9.4) Percentage male: 38.7 vs 40.1 Ethnicity: NR NYHA functional class intervention/control: NR Mean (SD) EF: 50.9 (16.6), N = 130 vs 48.3 (17.6), N = 124 Inclusion criteria: • all participants had been hospitalised for HF • lived in area covered by the collaborating home care unit • sufficient family support Exclusion criteria: • severe cognitive deficits • advanced psychiatric disease • non-cardiological terminal disease • COPD
Interventions	Duration of intervention: 15 days Intervention:

Aldamiz-Echevarria 2007 *(Continued)*

	• home visits by physicians and nurses, for clinical examination, tests/analyses as required, and adjustment of medication as required (N.B. this intervention was not HF-specific, but was intended to reduce readmissions across a range of medical and surgical conditions) • additional nursing staff home visits 2, 5 and 10 days after discharge for education for participants and relatives about HF (basic facts and management, i.e. symptoms, life style, diet and therapy) • participants received educational manual and a phone number for queries Compatator: • usual care (referral to primary care physician)
Outcomes	Primary: cumulative unplanned readmission or death 6 and 12 months after discharge Secondary: • cumulative unplanned readmissions • cumulative mortality • duration of readmission • use of emergency services during 1st 6 months after discharge
Notes	Data source: published data only Planned admissions were not considered events Funding/CoI: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Closed envelopes prepared by the Instituto de Ciencias de la Salud. The randomisation process was stratified with respect to the services involved (internal medicine, cardiology and short-stay).
Allocation concealment (selection bias)	Low risk	The sequence was concealed until interventions were assigned.
Blinding of participants and personnel (performance bias)	High risk	Quote: “By the very nature of the intervention being tested, neither the patients taking part in this study nor the home care unit personnel were blind to their treatment.”
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: “... staff attending them in other services were unaware of whether patients belonged to the programme or control group. Events assignment was, therefore, blinded.”
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "There were no dropouts from the study."
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Atienza 2004

Methods	Multicentre RCT (3 centres) Recruiting: January 1999- June 1999 Follow-up: median duration 509 days (IQR 365-649) Intervention category: case management Person delivering the intervention: cardiologist
Participants	Country: Spain Participants: 164 in intervention group, 174 in usual-care group Median age (IQR) 69 (61-74) in intervention group, 67 (58-74) in usual-care group Male sex (both groups) 203 (60%), (intervention group 101/164, 62%), (control group 102/174, 59%) Ethnicity: NR Actual severity of HF in study participants at recruitment (NYHA class, N): • intervention group: class I, N = 11; class II, N = 39; class III, N = 40; class IV, N =10 • control group: class I, N = 10; class II, N = 40; class III, N = 40; class IV, N = 10 Median EF% (IQR): intervention 36 (30-53); control 40 (30-55) Inclusion criteria: • all patients with congestive HF discharged from cardiology wards of 3 hospitals in Spain • HF diagnosis based on the presence of symptoms and signs of HF with objective evidence of major cardiac dysfunction at rest • All patients had been hospitalised for HF Exclusion criteria: • expected survival < 3 months • discharge to a nursing home or long-term care facility • living > 30 km from hospital • impossible to contact by phone • dementia or psychiatric illness • on a waiting list for invasive cardiology or heart surgery on discharge
Interventions	Median duration of intervention: 509 days (IQR 365-649) Intervention: discharge and outpatient management programme • 1-to-1 single education session for participants and carers prior to discharge and session with primary care physician post discharge to reinforce education • teaching brochure to reinforce education, covering: diagnosis of HF, information about the disease (pathogenesis etc), symptoms of HF, symptoms and signs of worsening HF, what to do if condition worsens, lifestyle advice, medication education for carers • cardiologist outpatient clinic every 3 months, including medication review • participant given specific/tailored self-management plan • visit with primary care physician scheduled within 2 weeks of discharge • telemonitoring component; a facilitated telephone monitor (SCT) providing a 24-h mobile phone contact number which participants were encouraged to contact as necessary. Participants could also telephone the HF team for advice during office hours Comparator:

Atienza 2004 *(Continued)*

	• discharge planning according to the routine protocol of the study hospitals
Outcomes	Primary outcome: event-free survival (survival without readmission to hospital) at 1 year Secondary outcomes: total number of hospital admissions (all-cause and for HF) at 1 year Other outcomes: readmission rate (all-cause and for HF); HRQoL (MLHFQ); costs; rate of deaths per observation year; time to readmission (all-cause + HF); time to death
Notes	Data source: published data only Funding: "Dr. Atienza was funded by the Spanish Society of Cardiology, Madrid, Spain. Prof. Martinez-Alzamora was funded by a Research Incentive Program from the Polytechnic University of Valencia, Spain. Merck, Sharp & Dohme contributed financially to the edition and printing of the brochure for HF patients used in the study"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	An independent assistant allocated participants using a computer-generated randomisation list. Block stratified randomisation performed according to age and sex
Allocation concealment (selection bias)	Unclear risk	No further details
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information on whether objective outcome assessment was blinded
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Data analysed on ITT principles, "one patient in each arm transferred to a nursing home during the study so their data were included in analyses but censored at time of transfer"
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified, beyond a slight baseline imbalance: more control participants had valvular heart disease (47/174 compared with 31/164) and fewer were on a beta blocker 20/174 compared with 31/164)

Bekelman 2015

Methods	Multicentre RCT (4 centres) Recruiting: May 2009-June 2011 Duration of follow-up: 12 months

Bekelman 2015 *(Continued)*

	Intervention category: multidisciplinary Person delivering intervention: "Each site had a collaborative care team consisting of a nurse coordinator (registered nurse), a primary care physician, a cardiologist, and a psychiatrist."
Participants	Country: USA Participants: N = 392 randomised (193 intervention, 199 usual care) Mean ± SD age: intervention: 67.3 (9.6); usual care: 67.9 (10.6) Male sex N (%): intervention: 178 (95.2); usual care: 193 (98.0) Ethnicity: N (%) intervention: 149 (79.7) white; control: 165 (83.8) white Actual severity of HF in study participants at recruitment (LVEF (%)): • intervention: data available for N = 171: normal 78 (45.6), mildly reduced 34 (19.9), moderately reduced 46 (26.9), severely reduced 13 (7.6) • usual care: data available for N = 177: normal 84 (47.5), mildly reduced 34 (19.2), moderately reduced 32 (18.1), severely reduced 27 (15.3) NYHA class (N (%)): • Intervention: class I, N = 16 (8.9%); class II, N = 77 (42.8%); class III, N = 82 (45.6%); class IV, N = 5 (2.8%) • Control: class I, N = 16 (8.5%); class II, N = 85 (45.0%); class III, N = 82 (43.4%); class IV, N = 6 (3.2%) Comorbidities • hypertension: intervention: 158 (84.5); control:159 (80.7) • diabetes: intervention: 99 (52.9); control: 93 (47.2) Inclusion criteria: (1) a primary inpatient hospital discharge diagnosis of HF (2) at least 2 secondary inpatient hospital discharge diagnoses of HF and a primary inpatient hospital discharge diagnosis related to heart disease; (3) at least 3 secondary inpatient hospital discharge diagnosis codes related to HF; (4) at least 2 outpatient visit diagnoses of HF, excluding emergency department visits; and (5) at least 2 secondary inpatient hospital discharge diagnoses of HF and at least 1 outpatient HF diagnosis. Exclusion criteria: (1) severe cognitive or psychiatric impairment; (2) current residence in a nursing home; (3) irreversible, noncardiac medical conditions likely to affect 6-month survival or ability to execute the study protocol; (4) prior heart transplantation; and (5) alcohol abuse
Interventions	Intervention: "The intervention included 3 components. These were multi-disciplinary collaborative care HF disease management, screening for and treatment of depression, and telemonitoring with patient self-care support." "For each intervention patient, the team reviewed the electronic health record and baseline depression scores from the Patient Health Questionnaire 9 (PHQ-9). The team recommended care changes for a given patient in accord with the American College of Cardiology and American Heart Association Guidelines for the Diagnosis Research Original Investigation Patient-Centered Disease Management for Heart Failure Trial and Management of Heart Failure in Adults and the collab-

Bekelman 2015 *(Continued)*

	orative depression care intervention as described herein. In addition, the team met weekly to recommend care changes based on review of telemonitoring data and the follow-up PHQ-9 score." "Intervention patients who screened positive for depression (PHQ-9 score, ≥10) received the depression care component of the intervention, adapted from a successful collaborative depression care intervention." "Intervention patients received daily telemonitoring using home-based equipment that tracked signs and symptoms ofHF and depression. The system collected daily measures of blood pressure, pulse, weight, and self-reported symptoms (eg, shortness of breath and edema). Patients with depression were asked questions about their mood and behavior. The telemonitoring system assigned a risk to each response on the system. The nurse reviewed medium risk indicators and decided whether an action needed to be taken (eg, for patients unable to understand a low sodium diet, the nurse provided counseling). The nurse acted on all of the high risk indicators by contacting the patient for assessment and then, if necessary, contacted the care team for any changes in medications or tests to be written in the electronic medical record." Comparator: "Patients randomized to the usual care arm continued to receive care from their regular health care professionals and regular telehealth nurses (if enrolled in telemonitoring), with no involvement of the study collaborative care team. Care was fully at the discretion of the patient's regular health care professionals and may or may not have included cardiology or mental health clinic care in addition to primary care. Usual care patients were given information sheets at the enrollment visit that described self-care for HF and were provided with a weighing scale if needed."
Outcomes	All-cause mortality All-cause readmissions HRQoL (KCCQ) Cost-effectiveness planned but NR
Notes	Funding/support: "The Patient-Centered Heart Failure Trial was funded by grant IIR 06-068 from the Department of Veterans Affairs Health Services Research and Development. Dr Bekelman was supported by Career Development Award 08-022 from the Department of Veterans Affairs Health Services Research and Development during this study. Role of the Funder/Sponsor: The Department of Veterans Affairs had no role in the design and conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The study database was used to create the randomization sequence using block randomization, with stratification by study site and 1:1 randomization of patients to the intervention and to usual care"
Allocation concealment (selection bias)	Unclear risk	Quote: "The randomization sequence was concealed from the study personnel. Randomization occurred after baseline survey information was entered into the database."
Blinding of participants and personnel (performance bias)	High risk	Quote: "unable to blind participants"
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Blinding unclear for nurse co-ordinator who collected outcome data at 12 months
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	A research assistant who collected QoL data was blinded, but QoL was self-reported by unblinded participants

Bekelman 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	6 intervention and 2 control participants dropped out at randomisation, and couldn't be included in results. Trial registry indicates that data were otherwise reported for all randomised people, including those who later dropped out/couldn't be contacted, but published paper's analysis appears to be of 165/193 intervention participants and 172/199 control participants
Selective reporting (reporting bias)	Unclear risk	Protocol published after end of trial, but registered prospectively on clinicaltrials.gov. 2 secondary outcomes planned but NR
Other bias	Low risk	Nothing detected

Berger 2010

Methods	Multicentre RCT (8 centres). 3 arms – only multidisciplinary care and usual-care groups are discussed here, since the BM arm (N-Terminal Pro-B-Type Natriuretic Peptide-Guided, Intensive Patient Management in Addition to Multidisciplinary Care) was not relevant to this review Recruiting: July 2003-September 2004 Duration of follow-up: 12 months Intervention category: case management Person delivering the intervention: multidisciplinary
Participants	Country: Austria Participants: N = 186: 96 in intervention group, 90 in usual-care group Mean ± SD age: 73 ± 11 in intervention group, 71 ± 13 in usual-care group Male sex: intervention 66/96 (68.8%); usual-care 59/90 (65.6%) Ethnicity: NR Actual severity of HF in study participants at recruitment: NYHA class NR Inclusion criteria: • hospitalised due to HF • clinical signs and symptoms of cardiac decompensation during the present hospitalisations • NYHA functional class III or IV at admission • cardiothoracic ratio > 0.5 or LVEF < 40% as documented by echocardiography Exclusion criteria: • NR
Interventions	Intervention: • multidisciplinary care by a specialised HF nurse, which included 4 home visits and telephone contact, 2 pre-scheduled consultations from the HF specialist 10 days and 2 months after discharge, and consultations on demand that were performed if any deterioration in the participant's status was noted by the HF nurse. Consultations included physical examination and laboratory testing of blood chemistry and blood cell count, and optimisation of medical therapy based on these. • Nurse care consisted of 4 home visits at 1, 3, 6, and 12 months after discharge by a nurse specialised in caring for people with HF. The nurse checked and recorded weight, symptoms and signs of HF, heart rate and blood pressure, and reviewed blood analyses on demand. In co-ordination with the HF specialist, the nurse checked for and implemented guideline-based HF medication. Nurse provided individualised patient and caregiver education and self-management advice.

Berger 2010 *(Continued)*

	Comparator: • usual care. Participant's management plan sent to primary care physician, who was responsible for patient evaluation and treatment, including assessing need for readmission. In hospitals in which the usual patient management offered visits for selected patients at the cardiac outpatient clinic, the discharging physician was allowed to arrange such visits as usual. Contact with the HF specialists of the research team was discouraged. Neither a structured follow-up nor specialised HF nurses were available for participants in the usual-care group
Outcomes	Pilot study so no primary outcome specified. End points included HF rehospitalisation, duration of time it takes to reach the combined end point of death and HF rehospitalisation, the first HF rehospitalisation, and death Cost utility analysis published by Moertl et al. 2013 (see Berger 2010)
Notes	Funding: "This study was funded by AstraZeneca, Novartis, Roche Diagnostics, Roche Medical, Merck, Medtronic, and Guidant, who provided the financial support for a clinical investigator, a specialised chronic HF nurse, and data collection."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomised to groups using computer-generated permuted block randomisation (6 participants per block)
Allocation concealment (selection bias)	Low risk	At discharge, concealed allocation was performed by sending the baseline characteristics of each participant to an independent medical project management institute
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: “Independent data collectors obtained information from medical reports and from interviews with relatives during the follow-up at least every 3 months. During a consensus reading, 2 cardiologists, who were blinded to the treatment groups, classified the cause of rehospitalization as being a result of cardiac decompensation or not. If the cause of rehospitalization was classified unclear by 1 cardiologist, the data collector provided the appropriate hospital charts for final classification."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No subjective outcomes reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss to follow-up
Selective reporting (reporting bias)	Unclear risk	NCT record registered after enrolment was completed, no published protocol identified
Other bias	High risk	NCT record suggests trial terminated, but no reason given for early stoppage. Generally similar at baseline, but 18/96 intervention vs 31/90 usual-care participants had mild-moderately reduced LVSF and 73/96 intervention vs 61/90 usual-care participants had severely reduced LVSF

Bernocchi 2017

Methods	Multicentre RCT (3 rehabilitation hospitals) Recruiting: July 2013-October 2014 Duration of follow-up: 6 months Intervention category: multidisciplinary Person delivering intervention: multidisciplinary (nurse and physiotherapist)
Participants	Country: Italy Participants: randomised N = 112 (N = 56 intervention, N = 56 control) Mean ± SD age: intervention: 71 (9); control 70 (9.5) Male sex N (%): intervention 50 (88%); control 42 (75%) Ethnicity: NR Participants in this trial had both HF and comorbid COPD Actual severity of HF in study participants at recruitment (NYHA class, N (%)): • intervention: class II, N = 25 (45%); class III, N = 22 (39%); class IV, N = 9 (16%) • control: class II, N = 29 (52%); class III, N = 19 (34%); class IV, N = 8 (14%) Inclusion criteria: • aged > 18 years • COPD GOLD classification, classes B, C, and D • systolic and/or diastolic HF NYHA classes II, II, and IV • ≥ 1 hospitalisation or visit due to HF or COPD exacerbation in the previous 12 months • signed informed consent The confirmed diagnosis of HF (NYHA class II-IV) and COPD (B, C and D GOLD class) had to be documented by an echocardiogram (HF) and by a spirometry examination (COPD) performed within the previous 12 months. The majority of participants had been hospitalised for HF as the first diagnosis. Of the 112 participants enrolled, 76 of them had as first diagnosis HF Exclusion criteria: • physical activity limitations due to noncardiac and/or pulmonary conditions • limited life expectancy • severe cognitive impairments
Interventions	Intervention: • educational intervention from a nurse tutor and a physiotherapist tutor, who then followed participants for 4-month telerehabilitation phase • weekly structured phone call from nurse tutor to collect information about disease status and symptoms, offering advice regarding diet, lifestyle and medications, previously defined with the cardiologist and pulmonologist supervising the programme • participants were provided with a pulse oximeter and a portable 1-lead electrocardiograph) for real-time telemonitoring of vital signs • participants could call in the case of urgent need or emergency 24 h/day 365 days/year • physiotherapist tutor designed a personalised exercise programme for each participant; who was provided with mini-ergometer, pedometer and diary. • physiotherapist tutor instructed participants and their caregivers on how to perform the exercises correctly, focusing on the rehabilitation goals. The number/intensity of training sessions according to participants' progress were adjusted during 4 months or in the case of problems

Bernocchi 2017 *(Continued)*

- there was a 'basic level' and 'high level' programme, physiotherapist tutor assessed participant to decide which to use
- physiotherapist tutor phoned each participant weekly to verify the training level of physical activity performed, plan the rehabilitation targets for the following week and give extra reinforcement on the value of lifestyle changes and the importance of exercise.

Comparator:

- participants received the standard care programme (including medications and oxygen prescription, visits from GP, and in-hospital check-ups on demand). At enrolment, participants received an educational session about healthy lifestyle and daily physical activity. Study author confirmed that this should be considered as standard care (26.6.18)

Outcomes	All-cause mortality; CV-related readmissions (but not HF readmissions); all-cause readmissions (total not number with readmission); QoL (MLHFQ)
Notes	Funding: Ministero della Salute (Italian Ministry of Health). The funding source did not influence or comment on planned methods, protocol, data analysis or the draft report. Study author supplied unpublished data for change from baseline to 6 months, and confirmed that the majority of participants had been hospitalised for HF as the primary diagnosis. Published and unpublished data. Searches identified the published protocol, study author sent the published paper (published after search date) and also sent the unpublished data on change in quality of life from baseline to 6 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated tables to allocate patients in fixed blocks of 4"
Allocation concealment (selection bias)	Low risk	Quote: "the allocation sequence was concealed from the investigators enrolling and assessing patients, in sequentially numbered, opaque, sealed envelopes."
Blinding of participants and personnel (performance bias)	High risk	Quote: "Due to the nature of the trial, it was not possible to blind patients and healthcare personnel to intervention."
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "outcome assessors and data analysts were blinded to the allocation."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported by participants who knew their allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Low overall (majority of participants accounted for for readmissions and mortality) High for QoL, as 80% of intervention group and 63% of control group completed this outcome - imbalance could lead to bias.
Selective reporting (reporting bias)	Low risk	Outcomes stated in trial registry published prior to study completion, match the outcomes of interest in the publications. Study author provided additional data for baseline to 6 months, as this had only been published as 0-4 months and 4-6 months.

Bernocchi 2017 *(Continued)*

Other bias	Low risk	Quote: "We tried to standardise as much as possible the nursing and physiotherapy approach in the three hospitals involved in the enrolment of patients, conducting joint training of staff, organisational meetings and planning before commencing patient enrolment."

Blue 2001

Methods	Single-centre RCT Recruiting: March 1997-November 1998 Duration of follow-up: 12 months (mean follow-up) Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: Scotland (UK) Participants: 81 participants (41 men, 51%) in comparison group, 84 (54 men, 64%) in intervention group Actual age of study participants: intervention 74.4 years (SD 8.6); usual-care mean 75.6 years (SD 7.9) Male sex: 58% Ethnicity: NR Actual severity of HF in study participants at recruitment (NYHA class, N (%)): • intervention group: class II, N = 19 (23%); class III, N = 28 (34%); class IV, N = 36 (43%) • control group: class II, N = 16 (20%); class III, N = 33 (42%); class IV, N = 30 (35%) LVEF: NR Inclusion criteria: • patients admitted as an emergency to the acute medical admissions unit at 1 hospital with HF due to LV systolic dysfunction. • all patients had been hospitalised for HF Exclusion criteria: • unable to give informed consent or to comply with the intervention • acute MI (unless they had a previous history of HF) • co-morbidity (such as advanced malignancy) likely to lead to death or readmission in the near future • awaiting cardiac surgery • planned discharge to long-term residential care • residence outside the hospital catchment area
Interventions	Duration of intervention: up to 12 months Intervention: "Specialist nurse intervention" During index hospitalisation: • participants were seen by a HF nurse prior to discharge After discharge: • home visit by HF nurse and within 48 h of discharge • subsequent visits by HF nurse at 1, 3, and 6 weeks and at 3, 6, 9 and 12 months. • scheduled phone calls at 2 weeks and at 1, 2, 4, 5, 7, 8, 10 and 11 months after discharge.

Blue 2001 *(Continued)*

- participants and their families encouraged to contact nurses with problems or questions by phone during office hours (answering machine where they could leave messages after hours)
- additional unscheduled home visits and telephone contacts as required

Home visits covered:

- participant education about HF and its Rx, self-monitoring and management (especially the early detection and treatment of decompensation)
- participants were given a booklet about HF which included a list of their drugs, contact details for HF nurses, blood test results and clinic appointment times
- trained HF nurses used written drug protocols and aimed to optimise participant treatment (drugs, exercise and diet)
- HF nurses also provided psychological support to the participant
- HF nurses liaised with the cardiology team and other healthcare and social workers as required

Comparator:

- usual care
- "Patients in the usual care group were managed as usual by the admitting physician and, subsequently, general practitioner. They were not seen by the specialist nurses after discharge."

Outcomes	Primary endpoints: • unplanned readmissions within 90 days of discharge • total number of days hospitalised during follow-up (12 months) Also looked at: • readmission rates in the moderate-risk subgroup compared to the high-risk sub group
Notes	Data source: published data only Funding: "This study was supported by a grant from the Scottish Office, Department of Health. Competing interests: None declared."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Study nurses phoned the Robertson Centre for Biostatistics and the patient was allocated to one or other randomisation group from a randomisation list."
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "We obtained data on admissions and deaths from the hospital records department, the information and statistics division of the Scottish NHS (hospital admissions) and the Registrar General's Office, Scotland (deaths). All hospital admissions were adjudicated blind to treatment allocation."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No subjective outcomes reported

Blue 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 1 person withdrew
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Bohmer 2011

Methods	Single-centre RCT Recruiting: November 2006-July 2008 Duration of follow-up: 6 months Intervention category: clinic Person delivering the intervention: multidisciplinary
Participants	Country: Austria, setting outpatient department plus phone calls to participant's home Participants: 140 (70%) intervention group, 60 (30%) usual-care group Mean age 68.3 years in intervention group, 73.4 in usual-care group Male sex: intervention group 77%, usual-care group 62% Ethnicity: NR Actual severity of HF in study participants at recruitment (NYHA class, %): • intervention group: class I, 21%; class II, 47%; class III, 30%; class IV, 2% • control group: class I, 23%; class II, 57%; class III, 20%, class IV, 0% LVEF %: intervention 32%, usual care 33% Inclusion criteria: • patients with chronic HF (LVEF < 40%) Exclusion criteria: • severe non-cardiac illness with a life expectancy < 1 year; • severe disability that would make ambulatory care impossible; • planned heart surgery
Interventions	The 'Kremser Model' involved education and training, testing, stepwise optimisation of drug therapy with the aim of achieving recommended target doses, regular outpatient visits to the hospital HF clinic (every 4 weeks) as required and regular phone calls by a trained HF nurse to check if drugs were tolerated and taken as prescribed or if other problems had arisen. The usual-care group were discharged from hospital with usual procedures of referral to GP and internal medicine specialist, with recommendation to adjust medication according to guidelines
Outcomes	No specification of primary outcome Outcomes: • mortality

Bohmer 2011 *(Continued)*

- adjustment of medication to target dose
- NYHA score
- well-being
- LVEF
- B-type natriuretic peptide

Notes	Funding: NR. CoI: study authors declare no conflict of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information in paper
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information given
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No subjective outcomes included
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	8% of the intervention group and no participants in the control group left the study (but intervention group was twice the size of control group). No information on whether their data were included in the analysis
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	There were some imbalances at baseline in this pilot study (age 68.3 (I) vs 73.4 (C); 23% female (I) vs 38% (C)

Brotons 2009

Methods	Multicentre RCT (4 hospitals) Recruiting: January 2004-September 2005 Duration of follow-up: 1 year Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: Spain, participants recruited from 2 university hospitals and 2 community hospitals for a home-based intervention Participants: N = 283 randomised, 144 to intervention, 139 to control Mean (SD) age: intervention: 76.6 (7.5) control: 76 (8.9)

Brotons 2009 *(Continued)*

	Male sex: intervention: 66 (45.8%), control: 61 (43.9%) Ethnicity: NR Actual severity of HF in study participants at recruitment (NYHA at hospital discharge (class, N, %)): • intervention: class I, N = 61 (42.2%); class II, N = 75 (52.1%); class III, N = 7 (4.9%); class IV, N = 1 (0.7%) • control: class I, N = 77 (55.4%); class II, N = 52 (37.4%); class III, N = 8 (5.8%); class IV, N = 2 (1.4%) Inclusion criteria: • no age limits • either sex • hospitalised for suspected HF based on dyspnoea with signs of pulmonary or systemic hypertension, consistent with the Framingham criteria (2 major criteria, or 1 major and 1 minor criterion were required) • diagnosis at hospital discharge had to show HF in the first or second position Exclusion criteria: • concomitant diseases and an expected survival of < 1 year • cognitive deficit • possibility of being outside the geographic area during the following year • participation in a clinical trial within the previous 3 months
Interventions	Intervention: • pre-discharge information about disease and treatments, with a participant booklet on HF • monthly home visits for 1 year (including education and recognition of warning symptoms, assessment of adherence to prescribed medication and lifestyle habits, plus checking of functional status and vital signs) • telephone calls from nurse every 15 days to evaluate clinical status • nurses contacted the participant's family physician or cardiologist when they deemed it was necessary to start a new treatment or modify the existing one Control: • participants randomised to the usual care were referred to their family physician and/or referral cardiologist
Outcomes	Primary: combination of all-cause death and hospital readmissions due to worsening of HF. Secondary: • CV death • hospital readmissions due to CV disease (hospital emergencies not considered) • QoL (MLHFQ, adapted for use in Spain) • adherence to therapy • satisfaction
Notes	Funding: "This study was funded by a subsidy from the Agència d'Avaluació de Tecnologia i Recerca Mèdiques (084/03/02), a research grant from the Acadèmia de Ciències Mèdiques i de la Salut de Catalunya i Balears (2005), and unrestricted funds from Novartis, Pfizer, Almirall-Prodesfarma, AstraZeneca, and Sanofi-Synthelabo. "

Risk of bias

Bias	Authors' judgement	Support for judgement

Brotons 2009 *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomisation was performed by computer, stratified for each hospital
Allocation concealment (selection bias)	Low risk	At the end of each interview, the nurse telephoned a central data management site to request random assignment of participants
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The endpoints were assessed by a committee of clinical events, blinded to the patient's treatment group."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Potentially high risk for QoL as participant-reported outcome
Incomplete outcome data (attrition bias) All outcomes	Low risk	Low for events: only 1 participant lost to follow-up; high for QoL (101/133 in intervention group responded at 1 year, 97/129 in control group)
Selective reporting (reporting bias)	Unclear risk	Trial registration (ISRCTN35096435) was after enrolment started
Other bias	Low risk	Nothing identified

Capomolla 2002

Methods	Single-centre RCT Recruitment: January 1999-January 2000 Duration of follow-up: mean follow-up of 12 months Intervention category: other (day hospital) Person delivering the intervention: multidisciplinary
Participants	Country: Italy Participants: N randomised = 234:122 participants (102 men, 84%) in comparison group, 112 (94 men, 84%) in intervention group Actual age of study participants: mean age 56 years (SD 10) Male sex: 84% Ethnicity: NR Actual severity of HF in study participants at baseline: • NYHA class I-II/III-IV: 158/81 (68% I-II) • LVEF: 29% (SD 7) Inclusion criteria: • patients with HF referred for admission to the HF Unit at 1 centre or the Heart Transplantation Programme (unclear if at the same centre) • a diagnosis of HF supported by clinical history, physical signs and symptoms, and by LVEF < 40%

Capomolla 2002 *(Continued)*

- all participants had been hospitalised for HF

Exclusion criteria:

- None given

Interventions	Duration of intervention: not clear Intervention: • comprehensive HF outpatient management programme delivered by the day hospital During index hospitalisation: • cardiac prognostic stratification and prescription of individual tailored therapy following guidelines and evidence After discharge: • attendance at day hospital staffed by a multidisciplinary team (cardiologist, nurse, physiotherapist, dietician, psychologist and social assistant). Participant access to the day hospital, "modulated according to demands of care process" • care plan developed for each participant • tailored interventions covering: cardiovascular risk stratification; tailored therapy; tailored physical training; counselling; checking clinical stability; correction of risk factors for haemodynamic instability; and healthcare education • participants who deteriorated re-entered the day hospital through an open-access programme • day hospital also offered intravenous therapy, laboratory examinations and therapeutic changes as required • education given covered: knowledge about HF and drug treatments; and self-management, including daily weights, fluid restriction and nutrition Comparison Group: • usual care During admission: • cardiac prognostic stratification and prescription of individual tailored therapy following guidelines and evidence After discharge: • "The patient returned to the community and was followed up by a primary care physician with the support of a cardiologist"
Outcomes	Primary outcomes (evaluated at a mean of 12 months): • readmissions because of haemodynamic instability • deaths from cardiac causes • cardiac mortality and urgent heart transplant Secondary outcomes (evaluated at a mean of 12 months): • "Tailored therapy management" • QOL • NYHA functional class Also looked at: • cost utility of the 2 strategies

Capomolla 2002 *(Continued)*

	Not clear if analysis done on ITT basis
Notes	Data source: published data only Funding/CoI: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients referred to our HFU had a prognostic evaluation, their therapy was optimised, and they were then randomised to one of two management strategies."
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	After 12 months all participants were re-evaluated in the HF Unit and the day hospital is part of this unit
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	High risk	Not all the 112 participants in the intervention received all the components of the intervention: 76% received education and physical training; 47% received cardiovascular risk stratification; 45% received tailored therapy; 19% received multidisciplinary intervention. There were 49 "open access interventions" in the intervention group, which included interventions that would have required admission in the control group.

Cavusoglu 2017

Methods	Multicentre RCT (10 centres) Recruiting: March 2010-April 2013 Duration of follow-up: 6 months Intervention category: multidisciplinary Person delivering intervention: multidisciplinary
Participants	Country: Turkey Participants: randomised N = 248 (125 intervention; 123 control)

Cavusoglu 2017 *(Continued)*

Mean ± SD age intervention: 60.6 ± 14.3; control: 61.1 ± 13.2

Male sex (%): intervention 76%; control 70%

Ethnicity: NR
Actual severity of HF in study participants at recruitment

LVEF (%) mean (SD): intervention 27.4 ± 7.1; control: 26.2 ± 7.1
NYHA class III-IV (%): intervention 60%; control 61%

Diabetes: intervention35%; control 37%

Inclusion criteria:

- > 18 years
- discharged from hospital with a diagnosis of HF within 6 months of randomisation
- current symptoms of HF despite optimal medical therapy consistent with recent guidelines (ACEI or angiotensin receptor blocker, beta blocker, mineralocorticoid receptor antagonist, and diuretics)
- NYHA functional class II–IV
- LVEF < 40% as measured by transthoracic echocardiography

Exclusion criteria:

- severe renal failure requiring dialysis
- serum creatinine > 2.5 mg/dL
- severe COPD
- chronic or intermittent inotropic support
- acute coronary syndromes defined by progressive angina or chest pain at rest or new ECG changes and/or serial increase in cardiac troponin levels
- recent percutaneous coronary interventions (PCI), cardiogenic shock, hypertrophic cardiomyopathy, acute myocarditis, severe primary valvular heart disease, dysfunction of a prosthetic heart valve, pericardial disease
- pregnancy
- uncontrolled thyroid disease
- currently enrolled in another HF study
- life expectancy < 6 months

Interventions	Intervention: • a cardiologist and nurse provided education on HF management during discharge and gave participants an education booklet and digital home scales • a printed HF education booklet was prepared in to unify the education content between centres • 1 session of HF education was implemented by a cardiologist together with a nurse at randomisation, in which the primary educator was the cardiologist • participant education took almost 1 h (30 min by the cardiologist and 30 min by the nurse), or more if needed • phone calls from cardiologist or nurse at months 1, 3 • phone call or hospital visit at 6 months to collect clinical data and go over HF education material • also assessed adoption of life style changes and adherence to medications, and reminded participants about salt and fluid intake, weight monitoring, daily routine activities, and exercise training • correction of doses or regimen of medication were made by a cardiologist or a nurse under the supervision of a cardiologist. • participants were invited to come to the hospital if needed Baseline education included: • description, causes, symptoms, prognosis and treatment of HF • lifestyle changes: salt intake, fluid and alcohol intake, the importance of weight monitoring, managing weight gain, daily measurement of blood pressure, adherence to medications, participation in daily

Cavusoglu 2017 *(Continued)*

	routine activities, exercise training, recognition of worsening HF symptoms, and when to contact the cardiologist. Comparator: usual care • participants were discharged from hospital without receiving any education or follow-up instructions • prescriptions were given along with the suggestion of a follow-up office visit
Outcomes	• CV mortality (not specifically HF mortality) • all-cause mortality • all-cause readmissions • HF readmissions
Notes	Funding: "This study had been designed, supported and conducted by the Working Group on Heart Failure of the Turkish Society of Cardiology." Published data only. Study author (Cavusoglu) confirmed by email 27 June 2018 that data for HF-mortality are not available, only data for CV-mortality.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (performance bias)	High risk	Quote: "because of the design of this study, both patients and investigators could not be blinded to treatment groups"
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Study nurses collected data at phone follow-up
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Not applicable - QoL NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on losses to follow-up, ITT analysis conducted
Selective reporting (reporting bias)	Unclear risk	No protocol or clinical trials registry entry found
Other bias	Low risk	Nothing identified

Chen 2018

Methods	Single-centre RCT Recruiting: December 2013-June 2015 Duration of follow-up: 6 months

Chen 2018 *(Continued)*

	Intervention category: multidisciplinary Person delivering intervention: multidisciplinary
Participants	Country: China Participants: N = 62 randomised, intervention N = 31; control N = 31 Mean ± SD age: intervention 61.1 (14.2); control 62.4 (14.9) Male sex N (%): intervention 22 (71.0); control 15 (48.4) Ethnicity: NR Actual severity of HF in study participants at recruitment: LVEF (mean (SD)%): intervention 39.9 (13.4); control 47.1 (13.4) NYHA class N (%): • intervention: class II, N = 1 (3.2%); class III, N = 15 (48.4%); class IV, N = 15 (48.4%) • control: class II, N = 1 (3.2%); class III, N = 16 (51.6%); class IV, N = 14 (45.2) Diabetes: intervention 6 (19.4) ; control 8 (25.8) Inclusion criteria: • HF diagnosis with NYHA class II to IV • > 18 years old Exclusion criteria: • cognitive impairment (people with scores < 24 on the MMSE questionnaire • inconvenience of home visit • inaccessible by telephone • concurrent inclusion in another study • diagnosis of COPD • diagnosis of other diseases whose life expectancy is < 1 year • diagnosis of other conditions that would restrict participant's activity
Interventions	Intervention: follow-up by HF team (3 cardiologists, 1 coach nurse, 10 nurses, 1 dietician, 1 psychiatrist) • individualised discharge education with cardiologist (HF info, weight monitoring, when to contact for help, self-care, medication adherence, dietary advice • psychiatrist and dietician involved where necessary • physical exercise training, individually tailored • home visit by coach nurse 2 weeks after discharge to check changes in signs and symptoms • phone contact every 2 weeks by cardiologist to monitor physical exercise, check medication adherence, reinforce education • intensified education by coach nurse at 90 and 180 days, tailored to participant's understanding of HF and self-care • during outpatient clinic visits, the coach nurse delivered specialised education and physical exercise training based on the participant's QoL, physical performance, and self-care behaviours Comparator: usual care • a telephone call within 2 weeks after discharge by a nurse • 2 follow-up visits for adjustment of medications by a cardiologist at outpatient clinic at 90 days and 180 days after discharge. • contacts with the cardiologists and nurses on HF team were discouraged
Outcomes	• HF readmission

Chen 2018 *(Continued)*

	• all-cause readmissions • HRQoL (MLHFQ - Chinese version) Outcomes only reported for combined endpoint (death or hospitalisation) AT emailed study author 11 July 2018 for individual outcomes, no response
Notes	Funding: Chia Family Health Fellowship granted by the Yale-China Association; Fundamental Research Funds for the Central Universities of Central South University granted by the Central South University. No CoI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-generated randomisation list was created by a statistician for patient randomisation
Allocation concealment (selection bias)	Low risk	Randomisation list was generated by the statistician not the study team
Blinding of participants and personnel (performance bias)	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Nurses who recruited patients, collected patients' data, and administered questionnaires were blind to the patient randomization."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants themselves were aware of allocation, so self-reported MLHFQ not blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data appear to be reported for all participants, but mortality and readmissions only reported as composite outcome
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration found
Other bias	Unclear risk	The proportion of eligible patients was low (of 264 people diagnosed with HF, 202 were excluded before randomisation (90 declined to participate, 56 did not meet inclusion criteria, 51 lived too far away, 5 died). May limit generalisability

Clark 2015

Methods	Single-centre RCT Recruiting: NR Duration of follow-up: 9 months Intervention category: case management Person delivering intervention: specialist nurse
Participants	Country: USA

Clark 2015 *(Continued)*

Participants: randomised N = 50; intervention N = 25; control N = 25

Mean ± SD age: intervention 61.7 (10.3); control 63.0 (11.7)

Male sex N (%): intervention 9/25 (36%); control 15/25 (60%)

Ethnicity: intervention 20/25 (80%) white; control 20/25 (80%) white
Actual severity of HF in study participants at recruitment:
NYHA class N (%):

- intervention: class I, N = 3 (12%); class II N = 10 (40%); class III, N = 12 (48%)
- control: class I, N = 4 (16%); class II, N = 11 (44%); class III, N = 10 (40%)

Diabetes: 48% of all participants

Inclusion criteria:

- diagnosed with NYHA class I-III 28 systolic or diastolic HF
- aged ≥ 45 years
- willing to participate in a randomised 9-month study
- living at home independently
- able to speak, read, and write in English
- a score of at least 23 on the MMSE

Exclusion criteria:

- major CVD (e.g. stroke
- NYHA class IV HF

Interventions	Intervention: "this study was underpinned by the health promotion model and self-efficacy theory, and the APRN's support in building participants' self-efficacy was a key part of the intervention." • 100-page booklet containing 8 modules formed the main educational material: HF information, signs and symptoms, diet, lifestyle, medications; when to seek help; memory enhancement techniques; diet; exercise; stress; depression; self-management; goal setting. • participants also received a book on improving memory First 3 months: • education-support intervention delivered by APRNs with expertise in HF • meeting every 10–14 days for 1–1.5 h to present the educational content Next 3 months: • phone and/or email support by APRN but no visits (average contact was 5-15 min every 3-4 weeks • Final 3 months without contact with the research team • All participants received a USD 25 cash appreciation gift Comparator: "The control group received a loose-leaf notebook of selected pages containing information on health promotion for adults/older adults information obtained from the National Institute of Aging website; Centers for Disease Control and Prevention, American Cancer Society, and the American Geriatric Society. Sample topics were: fall prevention; crime and older adults; arthritis; and bladder control. No content about HF was included. Meetings were scheduled during the first 3 months depending on the needs and interest of the participant. No phone or email teaching was done. Instruments were completed at the same 4 time periods (baseline, 3 months, 6 months, and 9 months) and retention gifts were provided ($25 each testing period). Usual medical care was received. All participants were offered the chance to receive the intervention at the end of the study; the majority received it."

Clark 2015 *(Continued)*

Outcomes	• KCCQ; total score data extract higher scores reflect better QoL. A 5-point change in total score is a clinically important difference.
Notes	Funding: NIH/NINR Study author checked all participants' data and confirmed that the majority had been admitted to hospital for HF at least once.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	States 'randomized' with no further details. 2 participants who dropped out were replaced, NR whether allocation of these was randomised or not.
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Nurse delivered intervention and collected outcomes
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL was self-reported by participants who knew group allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "Two participants lost to follow-up were replaced (one moved out of state; the other moved and could not be located) and their data were eliminated from the analysis" - not clear which group they were from, or whether the replacement participants' data were included in the analysis.
Selective reporting (reporting bias)	Unclear risk	No protocol or trial registration identified
Other bias	Low risk	Nothing noted

Cline 1998

Methods	Single-centre RCT Recruitment: December 1991-October 1993 Duration of follow-up: 12 months Intervention category: clinic Person delivering the intervention: specialist nurse
Participants	Country: Sweden Participants: 190 participants; intervention: 80 (44 men, 55%); control 110 (57 men, 52%) Actual age of study participants: mean 75.6 years (SD 5.3) Male sex: 53% Ethnicity: NR Actual severity of HF in study participants at baseline:

Cline 1998 *(Continued)*

NYHA class, mean:

- intervention 2.6 (SD 0.7)
- control 2.6 (SD 0.7)

LVEF: 75% LVEF < 40%

- intervention mean 31.6% (SD 8.4)
- control mean 35.7% (SD 12.3)

Inclusion criteria:

- patients hospitalised primarily because of HF
- HF diagnosed on symptoms and signs with "at least one objective sign present on admission such as pulmonary rales, peripheral oedema, congestion on chest radiograph, or a third heart sound"
- aged 65-84 years

Exclusion criteria:

- the presence of other serious disease that either prevented participation or was expected to significantly influence QoL, morbidity or mortality in the following year
- foreseeable follow-up problems, including residence outside the hospital catchment area
- serious alcohol or drug abuse
- psychiatric disease
- inability to understand or answer study questionnaire
- participation in another clinical trial
- discretion of treating physician

Interventions	Duration of intervention: 12 months Intervention: "Management programme for heart failure" During index hospitalisation: • Patients received an education programme from HF nurse consisting of two 30 minute visits. After discharge: • 2 weeks after discharge participants and their families were invited to a 1-h group education session led by the HF nurse. which included an oral presentation by the nurse, and educational video and a question and answer session • participants were also offered a 7-day medication dispenser if deemed appropriate • participants were followed up at a nurse directed outpatient clinic and there was a single prescheduled visit by the nurse at 8 months after discharge • HF nurse was available for phone contact during office hours • participants encouraged to contact the study nurse at their discretion, if unsure, if diuretic adjustments did not ameliorate symptoms in 2-3 days, or if there were "profound changes in self management variables" • participants were offered cardiology outpatient visits 1 and 4 months after discharge The inpatient and outpatient education programme covered: • HF pathophysiology, pharmacological and non-pharmacological treatment • participants were also given guidelines for self-management of diuretics in the event of fluid overload or fluid depletion • participants were given a "heart failure diary" containing information on HF, list of HF medications, names and contact phone numbers for the HF clinic and in which to regularly record bodyweight, ankle circumference and HF symptoms Comparator: usual care

Cline 1998 *(Continued)*

	• participants "followed up at the outpatient clinic in the department of cardiology by either cardiologists in private practice or by primary care physicians as considered appropriate by the discharging consultant."
Outcomes	Primary endpoint: unclear, abstract states that main outcome measures were: • time to readmission • days in hospital • healthcare costs during 1 year Other endpoints: • QoL (at 1 year) using The Quality of Life in Heart Failure Questionnaire, Nottingham Health Profile and patients' global self assessment (all self-administered) Also looked at: • Deaths at 90 days - not included in this review as < 6 months • Event-free (i.e. death or readmission) survival at 90 days - not included in this review as < 6 months
Notes	Data source: published data only Funding: "The study was supported by grants from the Swedish Heart and Lung Foundation, the research foundation administered by Malmö University Hospital, and the Council for Health Care Research, Lund University."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated random allocation"
Allocation concealment (selection bias)	Low risk	Quote: "Patients were invited to participate and informed consent was given on the basis of information relevant to the allocated study group. This procedure avoided bias arising from control patients being informed of the intervention strategy."
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	No objective outcomes at 6 months
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-assessed
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All participants were accounted for and deaths were verified by hospital records or death certificates, but QoL is the only included outcome here, and it is not clear how many people completed this at follow-up.
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Other bias	Unclear risk	Slightly lower LVEF in intervention group at baseline: mean (SD) LVEF (%) intervention: 31.6 (8.4) < 0.05; control: 35.7 (12.3)

de Souza 2014

Methods	Multicentre RCT (2 centres) Recruiting: August 2009-April 2012 Duration of follow-up: 6 months Intervention category: case management Person delivering intervention: nurse
Participants	Country: Brazil Participants: randomised N = 252; intervention N = 123; control N = 129 Mean ± SD age: intervention 62 ± 14; control: 63 ± 12 Male sex N (%): intervention 75 (61.0%); control 83 (64.3%) Ethnicity: intervention 83 (67.5% white); control 81 (62.8% white) Actual severity of HF in study participants at recruitment: EF mean SD %: intervention 29.2 ± 8.2; control 30.1 ± 9.5 NYHA class N (%) • intervention: class I, N = 6 (4.8%); class II, N = 48 (39.0%); class III, N = 52 (42.2%); class IV, N = 14 (11.3%) • control: class I, N = 10 (7.7%); class II, N = 47 (36.4%); class III, N = 64 (49.6%); class IV, N = 11 (8.5%) Inclusion criteria: • Adult patients (≥ 18 years old) • LV systolic dysfunction (LVEF ≤ 45%) • admitted because of acute decompensated HF • diagnosis of acute HF was confirmed by the attending physician, and all enrolled participants had to be on i/v diuretic therapy and to present the expected HF signs and symptoms. Exclusion criteria: • an acute HF episode secondary to sepsis, myocarditis or MI • major communication barriers • residence > 20 km from the hospital • lack of the possibility of telephone contact
Interventions	Intervention: • 4 home visits, about 1 h each, 1st within 10 days of discharge, approx. days 30, 60 and 120 days after discharge • included physical examination, knowledge/self-care assessment and adherence to recommendations, medications, weight control, hydro-saline restriction, physical activity, vaccination, weight monitoring, signs and symptoms to watch for and therapeutic strategies. • consultant would adjust drugs where necessary • 4 reinforcement phone calls, about 10 min each both led by trained nurses, to reinforce the info given at the home visit, check use of medications, and clarify any issues • Outpatient clinic visit at 180 days follow-up to finalise assessment Comparator: usual care • medical outpatient visits in which they received instructions regarding pharmacological and non-pharmacological therapeutic strategies.

de Souza 2014 *(Continued)*

	• no specific management plan was applied and each hospital decided the approach for each participant. • Typically, participants were followed-up by a GP after hospital discharge. • No home visits or telephone contact
Outcomes	• All-cause mortality • HF readmissions • All-cause readmissions • Cost-effectiveness
Notes	Funding: Fundo de Incentivo à Pesquisa e Eventos do Hospital de Clínicas de PortoAlegre (FIPE); Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). No CoI Study author confirmed that this study (HELEN II) has the outcomes from the previously identified ongoing HELEN I study (a related paper by Mussi 2013 was previously excluded as no relevant outcomes reported)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple sequence randomisation was used, generated electronically on the website www.randomization.com
Allocation concealment (selection bias)	Low risk	Quote: "A healthcare professional who was not a member of the research group was responsible for the patient allocation list. The intervention nurses were blinded to the patients' allocation group until all instruments had been completed in the baseline period."
Blinding of participants and personnel (performance bias)	High risk	Not possible to blind
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	A nurse who was blinded to group allocation was responsible for the final evaluations and for assessment of clinical outcomes.
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Not applicable: QoL NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Study flow chart indicates all randomised participants included in follow-up (perhaps just for Kaplan Meir survival analysis?) Outcome table indicates 117/123 intervention participants and 126/129 control participants included in clinical outcomes at 6 months
Selective reporting (reporting bias)	High risk	Trial registered after it had started. NCT trial register states original primary outcome (2010) was to be absolute number readmissions and visits to ED for decompensation of HF. Changed in 2014 to a composite endpoint of a first visit to ED, or a first hospital readmission, or all-cause death
Other bias	Low risk	Nothing identified

DeBusk 2004

Methods	Multicentre RCT (5 centres) Recruitment: May 1998-October 2000 Duration of follow-up: 12 months Intervention category: case management Person delivering the intervention: nurse
Participants	Country: USA Number randomised: 462 (intervention N = 228, control N = 234) NYHA class, N (%) • intervention group: class I-II, N = 103 (50%); class III-IV, N = 103 (50%) • control group: class I-II, N = 112 (50%); class III-IV, N = 113 (50%) Median EF%: NR Mean age: all: 72 years (SD 11); • intervention: < 60 years: 35 (15%); 60-70 years: 52 (22%); 70-80 years: 92 (40%); > 80 years: 49 (21%) • control: < 60 years: 32 (14%); 60-70 years: 55 (24%); 70-80 years: 86 (37%); > 80 years: 49 61 (26%) Ethnicity, N (%): • intervention: white 195 (86); black 13 (5); American Indian 9 (4); Hispanic 7 (3); Asian 4 (2) • control: white 191 (82); black 14 (6); American Indian 18 (8); Hispanic 7 (3); Asian 4 (2) Inclusion criteria: • hospitalised with a provisional diagnosis of HF in study hospitals as indicated by new onset or worsening HF on the basis of shortness of breath (dyspnoea at rest, orthopnoea or paroxysmal nocturnal dyspnoea) Exclusion criteria: • scheduled for coronary artery bypass surgery or valvular surgery • undergone cardiac surgery in preceding 8 weeks • serum creatinine value ≥ 5 mg/dL • receiving dialysis • awaiting renal Tx • history severe pulmonary disease on home O2 • ≥ 1 additional diagnoses expected to result in death within the year • cognitive mental deficits • substance abuse • severe psychiatric disorders • expected to move from area within 1 year
Interventions	Duration of intervention: 12 months Intervention: "specialist nurse intervention" • I-h educational session with a nurse in the participant's medical centre • participant received printed educational materials including methods for self-monitoring symptoms, body weight and medications; a dietary management workbook; food frequency questionnaires • participants viewed a video portraying the treatment process

DeBusk 2004 *(Continued)*

- participants received instructions on how to access emergency care in case symptoms abruptly worsened
- 45-min baseline telephone counselling session within 1 week of randomisation by experienced nurse care manager
- subsequent nurse contacts tailored to meet needs of the participant
- nurse initiated follow-up phone calls to participant weekly for 6 weeks, biweekly for 8 weeks, monthly for 3 months, bimonthly for 6 months
- nurse care managers obtained permission from physicians to initiate and regulate pharmacologic therapy for HF according to study protocol
- nurses communicated with physicians about participant's medical status
- nurses co-ordinated treatment plan with participants and physicians

Comparator: usual care (no details given)

Outcomes	Outcomes (1 year) Primary outcome: • time to first hospitalisation HF and all-cause Secondary outcomes: • time to composite outcome of death, • readmission or ED visit for cardiac cause or for any cause • rate of outpatient and ED visits
Notes	Data source: published data only Funding: "The National Heart, Lung and Blood Insitute reviewed and financially supported the project but did not participate in the design, conduct, or reporting of the study or in the decision to submit the manuscript for publication." "Potential financial conflict of interest: none disclosed."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Research staff who were not associated with delivering the intervention randomly assigned participants to treatment conditions by using sealed assignments. Equal numbers of participants were allocated to the 2 groups in each medical centre using the Efron procedure.
Allocation concealment (selection bias)	Low risk	Research staff who were not associated with delivering the intervention randomly assigned participants to treatment conditions by using sealed assignments.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Research staff who were not associated with, and were blinded to, the intervention conditions measured health outcomes at 12 months. Two cardiologists who were not associated with implementing the intervention reviewed medical records on deaths, rehospitalizations, and emergency department visits to determine whether these events were primarily due to heart failure or due to other causes. They did not use discharge diagnoses recorded in the medical record to make these judgments."

DeBusk 2004 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No subjective outcomes reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Slightly unbalanced drop out rate (15/234 6% in usual care, 8/228 3.5% in intervention group) but ITT analysis used
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing noted

Del Sindaco 2007

Methods	Open RCT Recruitment: January 2001-December 2002 Duration of follow-up: 24 months Intervention category: multidisciplinary Person delivering the intervention: multidisciplinary
Participants	Country: Italy Number randomised: 184 (control N = 87, intervention N = 86) NYHA: • intervention: class I, N = 0 (0%); class II, N = 32 (37.2%); class III, N = 44 (51.2%); class IV, N = 10 (11.6%) • control: class I, N = 0 (0%); class II, N = 34 (39.1%); class III, N = 49 (56.3%); class IV, N = 4 (4.6%) LVEF: intervention: 33.5 (SD 11); control: 32.5 (SD 10) Age: intervention: 77.4 (SD 5.9); control: 77.5 (SD 5.7) Percentage male: intervention: 51.2; control: 52.8 Ethnicity: NR Inclusion criteria: • ≥ 70 years • discharged home after hospitalisation due to HF • NYHA III-IV for ≥ 24 h requiring i/v therapy on admission • diagnosis determined according to ECS guidelines Exclusion criteria: • valvular heart disease requiring planned surgical correction • active substance abuse • severe gait impairment • confined to bed • severe dementia • psychiatric disease likely to limit compliance • co-existent non-cardiac disease likely to reduce life expectancy • need for long-term i/v inotropic therapy

Del Sindaco 2007 *(Continued)*

- unwillingness to provide informed consent
- living in a nursing home
- Living outside the area served by the clinical sites

Interventions	Duration of intervention: 24 months Intervention: DMP combining hospital clinic-based and home-based care • teams included a cardiologist experienced in geriatrics, 2-4 specialised nurses and the participant's primary care physician • components of the programme were; discharge planning, continuing education, therapy optimisation, improved communication with healthcare providers, early attention to signs and symptoms and flexible diuretic regimes • participants given a written list of recommendations, a weight chart, a contact number available 6 h/day, and an education booklet • follow-up via hospital clinic visits, periodical nurse's phone calls • participants attended HF clinics within 7-14 days of discharge and at 1, 3 and 6 months thereafter for optimisation of treatment and education • primary care physicians assessed adherence to treatment, evaluated adverse effects and co-morbidities, and monitored diet Control: usual care • optimised treatment and standard education • all treatments and services ordered by primary care physician and/or cardiologist • baseline clinical evaluation and therapeutic plan documented
Outcomes	Primary: • composite of all-cause death and hospital admissions from HF at 24 months Secondary (24 months): • all-cause and HF hospitalisations • cumulative number of hospitalisations • all cause and HF related mortality • QoL • perceived health status • functional status and indexes of quality of care (such as % of participants taking beta-blockers) - not recorded here
Notes	Data source: published data only Funding/CoI: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No details given, just states "randomised"
Allocation concealment (selection bias)	High risk	Eligible patients were randomised and informed consent was given on the basis of information relevant to the allocated study group
Blinding of participants and personnel (performance bias)	High risk	Not possible

Del Sindaco 2007 *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Outcomes were evaluated in a blinded manner by a central endpoint committee composed of three cardiologists, who had no knowledge of the treatment assignment."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	All randomised participants included in table of outcomes at 2 years. Quote: "A relatively high rate of patients abandoned the hospital component of the programme and continued care with their primary care physicians and/or personal cardiologists. The participation of these patients until the end of the follow-up would have further improved the effects of intervention because, on intention-to-treat analysis, this high drop-out rate was not associated with a significant decline in the efficacy of the model."
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Doughty 2002

Methods	Single-centre, cluster-RCT, GP as the unit of randomisation (but see note) Recruitment: during 1997 and 1998 Duration of follow-up: 12 months Intervention category: clinic Person delivering the intervention: multidisciplinary
Participants	Country: New Zealand Participants: 97 participants; intervention 100 (64 men, 64%); control (54 men, 56%) Actual age of study participants: mean 73 years (SD 10.8, range 34-92 years) Male sex: 60% Ethnicity: 'NZ European' 79% Severity of HF in study participants at index admission: NYHA class, N (%) • intervention: class II, N = 24 (24%), class III, N = 76 (76%) • control: class II, N = 24 (25%), class III, N = 73 (75%) Severity of HF in study participants at baseline: LVEF • intervention group 30.6% (SD 12.7) • control group mean 33.8% (SD 12.7) Inclusion criteria: • Patients admitted to general medical wards with a primary diagnosis of HF Exclusion criteria: • surgically remediable cause for HF • consideration for heart transplantation • terminal cancer • participation in another trial

Doughty 2002 *(Continued)*

	• inability to provide informed consent
Interventions	Duration of intervention: 12 months Intervention: integrated heart failure management programme After discharge: • outpatient review at HF clinic within 2/52 of discharge from hospital: clinical status reviewed, pharmacological treatment based on evidence based guidelines, 1-to-1 education with study nurse, education booklet provided • participant diary for daily weights, Rx record and clinical notes provided • detailed letter faxed to GP and follow-up phone call to GP • GPs encouraged to discuss management with clinic team • Follow-up plan aiming at 6 weekly visits alternating between GP and HF clinic • Group education sessions for participants run by cardiologist and study nurse: 2 sessions offered within 6 weeks of discharge and 1 at 6 months post-discharge • telephone access to study team for GPs or participants during office hours Group education sessions covered: • education about disease • monitoring daily body weight and action plans for weight changes • medication • exercise • diet Comparison: usual care
Outcomes	Primary endpoints (12 months): • time to first event i.e. death or hospital readmission • HRQL measured using MLHFQ at baseline and 12 months Other endpoints (12 months): • all-cause hospital readmissions • HF hospital readmissions • all-cause hospital bed-days Also looked at: • medications at 12 months
Notes	Data source: published data only Funding: "The study was funded by a project grant from the National Heart of New Zealand and an unrestricted educational grant from Merck Sharp Dohme (NZ) Ltd. RND was the recipient of the New Zealand Heart Foundation BNZ Senior Fellowship. "

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "General practitioners were randomly allocated using computer generated random numbers…after consent was obtained the patient was informed of their group allocation based on the randomisation of their current general practitioner."

Doughty 2002 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	NR. GPs were randomised before participant recruitment - possibility that team were aware of assignment of GP before recruitment of patient into study
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only one participant lost to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	This was a cluster-RCT, but outcomes were reported for individual participants. Paper states that, Quote: "Data were analysed using two approaches. Firstly the unit of randomization was assumed to be the individual, as if simple randomization had been performed. ... In other analyses the unit of randomization was the GP, consistent with the actual method of cluster randomization. ...Since the median number of participants per general practitioner was small (1·5 in each arm) the influence of clustering was small and only results from the first approach are presented. In no case did statistical significance differ depending upon the approach adopted."

Ducharme 2005

Methods	Single-centre RCT Recruitment: January 1998- January 2000 Duration of follow-up: 6 months Intervention category: multidisciplinary Person delivering the intervention: multidisciplinary
Participants	Country: Canada Participants: intervention N = 115/control N = 115 Mean (SD) age: 68 (10)/10 (10) % male: 83 (73)/82 (71) Ethnicity: NR EF% (SD): 34 (14)/35 (15) NYHA class, N (%)

Ducharme 2005 *(Continued)*

	intervention: class II, N = 8 (7%); class III, N = 68 (59%); class IV, N = 39 (34%) control: class II, N = 14 (12%); class III, N = 63 (55%); class IV, N = 38 (33%) Inclusion criteria • seen at the ED of or admitted to the Montreal Heart Institute with a primary diagnosis of congestive HF • radiologic confirmation of congestive HF or known impaired LVEF (< 45%) Exclusion criteria: • a primary diagnosis of acute MI • discharge to a chronic care facility, scheduled cardiac surgery • unwillingness to sign informed consent or to attend the outpatient clinic • participation in another research trial • residence in an outlying area
Interventions	Duration of intervention: 6 months Intervention: multi-disciplinary HF clinic with phone follow-up from nurses • evaluation at clinic within 2 weeks of hospital discharge • HF clinic provided rapid access to cardiologists, clinician nurses, dieticians and pharmacists, with access to social workers and other medical specialists as required • clinic allowed observation for up to 5 h and i/v diuretics if required • follow-up phone call from nurse within 72 h of hospital discharge and then monthly, unless a problem necessitated more frequent contact • After baseline evaluation, clinic cardiologists individualised treatment plan (including pharmacologic treatment) for participants • 1-on-1 education of the participant and family with the study nurse initiated at 1st clinic visit. Individualised advice on the disease process, symptoms and signs of HF (changes in symptoms indicative of worsening HF), fluid and sodium intake restrictions, the importance of daily monitoring of body weight and action plans to remedy changes in weight, effects of medications and the importance of compliance, and recommendations regarding exercise and diet • participant diary for daily weight measurement,medication record, clinical notes and appointments, physical activity recommendations, an education booklet and a telephone number for clinic during business hours • individualised dietary assessments by registered dietician at baseline, instructions reinforced by nurse at subsequent visits • pharmacist evaluated medications for each participant and assessed participant's knowledge • individualised follow-up plan included monthly visits with both a cardiologist and nurse at the clinic • study team available for ad hoc consultation during normal working hours. Participants advised to call clinic nurse if symptoms worsened. During calls nurse evaluated signs of clinical deterioration and adverse effects and participants were referred to clinic cardiologist as required Comparator: usual care
Outcomes	Primary endpoints: • all-cause hospital readmissions • total number of associated hospital days at 6 months Secondary outcomes (at 6 months): • number of ED visits • QoL • mortality
Notes	Data source: published data only

Ducharme 2005 *(Continued)*

	Funding: "competing interests: none declared" but "James Brophy and Michel White receive support from les Fonds de la recherche en santé du Québec". "unrestricted educational grants from Merck Frosst and GlaxoSmithKline"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Eligible patients who agreed to participate were randomly assigned to the control group or intervention group using consecutively numbered opaque envelopes that contained a random number generating group assignment."
Allocation concealment (selection bias)	Low risk	Consecutively numbered opaque envelopes used
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "It is also possible that incomplete blinding of the data extractors may have introduced another bias. To minimize the potential impact of such a bias, we selected outcomes (repeat hospital admission and duration of hospital stay) that are not typically affected by subjective interpretations. The unblinding of the study physicians is also unlikely to have influenced hospital admission patterns since the physicians represent fewer than 10% of the cardiologists with admission privileges at the institution."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported by participants who knew allocation (although questionnaire administered by blinded personnel)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analyses were ITT
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Dunbar 2014

Methods	Multicentre RCT (4 centres) Recruiting: 2010-2013 Duration of follow-up: 6 months Intervention category: case management Person delivering intervention: research nurse
Participants	Country: USA Participants: N = 134 randomised (intervention N = 70; control N = 64) Age mean ± SD, range: intervention 57.7 (10.5), 31-81; control 57.0 (10.8), 29-76

Dunbar 2014 *(Continued)*

Male sex N (%): intervention 47 (67.1%); control 41 (64.1%)

Ethnicity N (%): intervention African American, 52 (74.3%); control African American, 41 64.1%)
Actual severity of HF in study participants at recruitment:

- LVEF (mean (SD) %): intervention 32.3 (16.6); control 35.7 (18.6)

NYHA class:

- intervention: class I, N = 1 (1.4%); class II, N = 28 (40.0%); class III, N = 36 (51.4%); class IV, N = 5 (7.1%)
- control: class I, N = 0 (0.0%); class II, N = 28 (43.8%); class III, N = 31 (48.4%); class IV, N = 5 (7.8%)

Diabetes: all participants had both diabetes and HF, as this was a specific inclusion criterion

Inclusion criteria:

- current or recent hospitalisation for HF within the past 3 months
- age 21-80 years
- NYHA functional class II-IV symptoms
- type II DM
- planned discharge to home and not to an assisted living or skilled nursing facility
- English language fluency
- baseline guideline-derived medical therapy unless there was documented contraindication, ambulatory and eligible for a walking physical activity programme,
- eligible for a low-sodium and low-carbohydrate diet

Exclusion criteria:

- newly diagnosed or 1st HF admission
- positive screenings for depressive symptoms and cognitive difficulty, which would interfere with ability to participate in the intervention or perform adequate self-care
- uncorrected hearing or vision problem
- undergoing cardiac transplantation or mechanical circulatory assist device implantation or evaluation at the time of enrolment
- renal failure requiring renal replacement treatment
- lack of telephone access
- severe COPD and earlier stroke if they impeded ability to ambulate

Interventions	Intervention: • individualised educational and counselling session by trained research nurse including: overview of HF and DM, self-care diet, medications, symptom monitoring; weight monitoring; physical activity • HF-DM tool kit provided for home use • home visit by research nurse 48-72 h later to review self-monitoring, reinforce information and assess diet and medication congruent with discharge instructions • scripted phone call at 7-10 days to review self-monitoring and check diet and medication, physical activity mentioned • 2 weeks – clinic visit that incorporated physical activity counselling • scripted phone calls at 1, 2 and 4 months to review and promote self-monitoring, diet, physical activity and medication-taking Comparator: usual car • after randomisation given publicly available informational brochures. Standard hospital discharge teaching from staff in the enrolling institutions and follow-up clinic appointments • control group participants received ‘‘attention control’’ telephone calls on the same schedule as the intervention participants with information about the trial, number of participants enrolled to date, and a reminder of their next set of study activities.

Dunbar 2014 *(Continued)*

Outcomes	• All-cause mortality • All-cause readmissions • HRQoL (MLHFQ) • Cost-effectiveness
Notes	Funding: NIH, NINR; National Center for Advancing Translational Sciences of the National Institutes of Health; Atlanta Veterans Administration Medical Center. No CoI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A table of random numbers was used to create group assignments that were placed in sealed envelopes until baseline data were collected."
Allocation concealment (selection bias)	Unclear risk	Sealed envelopes used, but doesn't specify that these are opaque and sequentially numbered.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-assessed
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear: imbalance in loss to follow-up, bias could affect completion of QoL assessments. Paper indicates that mutlilevel mixed models were run to adjust for attrition over time.
Selective reporting (reporting bias)	Low risk	Outcomes listed on trial registration site (after study initiation but before study completion) include MLHFQ
Other bias	Low risk	Nothing identified

Gonzalez-Guerrero 2014

Methods	Single-centre RCT Recruiting: March 2007-November 2009 Duration of follow-up: 12 months Intervention category: multidisciplinary team in geriatric day care hospital (categorised as multidisciplinary for this review) Person delivering intervention: multidisciplinary
Participants	Country: Spain Participants: randomised N = 120 (intervention N = 60; control N = 60; 1 intervention and 2 control discontinued post-randomisation but before intervention so have no baseline assessment)

Gonzalez-Guerrero 2014 *(Continued)*

Mean ± SD age: intervention 85 (6.4); control 85 (6.3)

Male sex N (%): intervention 17/59 (28.8%); control 15/58 (25.8%)

Ethnicity: NR
Actual severity of HF in study participants at recruitment: previous NYHA class, mean (SD):

- intervention 2.5 (0.7)
- control 2.3 (0.8)

Diabetes N (%): intervention 26 (44.1); control 19 (32.8)

Inclusion criteria:

- Consecutive patients diagnosed with acute HF and discharged from the Geriatric Service of the Cáceres Hospital Complex (Spain)
- diagnosis according to ESC criteria
- hospital stay of > 1 days

Additional information from trial registry:

- participants aged > 65;
- discharged home or to a nursing home without medical staff
- hospitalisation due to HF of ≥ 48 h (determined according to the ESC guidelines)

Exclusion criteria:

- terminal disease (expected survival < 6 months)
- bedridden
- severe dementia or other serious psychiatric disease
- impossible to follow-up
- in retirement homes with own medical service

Interventions	Intervention: • DMP multidisciplinary team (geriatrician (case manager), nurse, social worker) evaluated participants and their caregivers prior to the hospital discharge. • participants were given an information manual about the disease, diet, weight control, exercise, lifestyle, and medication, as well as how to recognize cardiac decompensation symptoms. • phone call from nurse 48 h after hospital discharge, to record any problems • After 10 days, the team examined the participants in the geriatric day-care hospital, using educational reinforcements and evaluating for possible cardiac decompensation • Follow-up at the geriatric day-care hospital 1 and 6 months after discharge. Team assessed treatment compliance, reinforced health education, and assessed participants' ability to fulfil recommendations; prescriptions and doses were adjusted according to clinical guidelines. Re-evaluation of global therapeutic regime and comorbidities considering possible changes in functional, cognitive, affective, and social capacities. • phone call from geriatrician during month 3. Geriatrician was also available by phone during 09:00-14:00, and all participants could receive attention in the hospital or via phone for unscheduled evaluation of clinical decline due to a medical problem • all follow-up involved health-educational reinforcement and evaluation of possible cardiac decompensation Comparator: • before the hospital discharge, each participant and the caregiver received an information manual explaining the HF education. • following hospital discharge, treatment and follow-up were provided by the primary care physician • visits were scheduled, and treatment was prescribed depending on the case

Gonzalez-Guerrero 2014 *(Continued)*

	• outpatient appointments at the Geriatric Service or other medical facilities were provided by non-members of the research study
Outcomes	• HF-mortality • All-cause mortality • HF readmissions • All-cause readmissions • HRQoL (MLHFQ) • Cost-effectiveness
Notes	Funding: Research Group Grant, co-financed by Regional Government of Extremadura (Spain) and European Union (FEDER). "The funder did not influence the design, methods, subject recruitment, data collections, analysis, or preparation of paper."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The patients were separated randomly using a computer-generated list."
Allocation concealment (selection bias)	Unclear risk	Quote: "Upon hospital discharge, the patients and the researchers ignored the group assigned to each patient."
Blinding of participants and personnel (performance bias)	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The results were obtained from the patients and their relatives, the hospital records, and the National Death Index.The result variables were adjudicated by a researcher of the Department of Patient Management, who was unaware of the group to which the patients belonged."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL participant-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analyses includes all randomised participants who received the intervention (excluding 1 intervention and 2 control participants who moved out of the area before receiving intervention). For MLHFQ, the missing values from censored cases were included. 3 participants were censored during the follow-up as they were hospitalised and referred to other medical services (2 from the intervention group and one from the control group)
Selective reporting (reporting bias)	High risk	Study registered retrospectively (ISRCTN10823032) with a different title, emphasising cost-effectiveness analysis as a co-primary outcome with event-free survival. No cost-effectiveness results published on trials registry or in literature to date.
Other bias	Low risk	Nothing identified

Holland 2007

Methods	Multicentre RCT (3 centres)

Holland 2007 *(Continued)*

	Recruitment: December 2003-March 2005 Duration of follow-up: 6 months Intervention category: case management Person delivering the intervention: community pharmacist
Participants	Country: UK Number randomised: 339 169 allocated to intervention, 170 to control 20 intervention and 26 control participants excluded post-randomisation. Study involved 149 intervention participants and 144 control group participants NYHA: • intervention: class I, N = 6 (4.0%); class II, N = 43 (28.9%); class III, N = 52 (34.9%); class IV, N = 48 (32.2%) • control: class I, N = 11 (7.6%); Class II, N = 37 (25.7%); class III, N = 47 (32.6%); class IV, N = 49 (34.0%) LVEF: NR Age: intervention: 76.4 (9.5); control: 77.6 (9.0) Percentage male: intervention: 63.2; control: 63.8 Ethnicity: NR Inclusion criteria: • adults (aged ≥ 18 years), admitted as an emergency in which HF was an important ongoing clinical condition, i.e. all participants had been hospitalised for HF • prescribed ≥ 2 drugs (from any drug class) on discharge Exclusion criteria: • living in a residential or nursing home • awaiting surgery for ischaemic or valvular heart disease • awaiting heart transplantation • terminal malignancy
Interventions	Duration of intervention: 6-8 weeks Intervention: community pharmacist home visits within 2 weeks of discharge, where • pharmacist provided education to participant and carer on HF, drugs, exercise, diet and smoking cessation, in line with British Heart Foundation's 'Living with Heart Failure' booklet *which was left with participants • participants encouraged to complete simple sign and symptom monitoring diary card (including weight) • pharmacist fed back recommendations to GP and any need for drug adherence aid to local pharmacist • An additional follow-up visit was made 6-8 weeks after discharge to review progress and reinforce original advice Control group: usual care
Outcomes	Primary: • total emergency admissions to hospital in 6 months Secondary:

Holland 2007 *(Continued)*

- deaths at 6 months
- QoL (EQ-5D) and MLWHF at 6 months

Notes	Data source: published data only Funding: "Research costs were funded by a project grant from the British Heart Foundation. Excess treatment costs were funded by Great Yarmouth and Southern Norfolk Primary Care Trusts. This trial received support for the educational training events from Pfizer UK." CoI: none declared

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “We used third party telephone randomisation based on a computer generated random allocation sequence.”
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Emergency admission data came from Hospital Episode Statistics. The Office for National Statistics provided mortality data".
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "We analysed patient data according to randomisation group, irrespective of whether or not they received the intervention as planned (the intention to treat principle)." but flow chart indicates only 148/169 (87.6%) intervention group and 143/170 (84%) control group analysed
Selective reporting (reporting bias)	Unclear risk	Trial retrospectively registered: ISRCTN59427925
Other bias	Low risk	Nothing identified

Jaarsma 2000

Methods	RCT Recruitment: May 1994-March 1997 Duration of follow-up: 9 months Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: the Netherlands Participants (patients enrolled and surviving to discharge): 84 participants in intervention group* 95 participants in comparison group

Jaarsma 2000 *(Continued)*

	Actual age of study participants: NR for original group, those who remained at 9 months were mean age 72 years (SD 9) at baseline Male sex: of those who remained at 9 months, 60% Ethnicity: NR Actual severity of HF in study participants at recruitment: NR Inclusion criteria: • participants admitted to the cardiology unit of 1 hospital with HF symptoms and diagnosis verified with Boston score • NYHA III or IV • HF diagnosis for > 3 months • Aged ≥ 50 years • Dutch literate Study exclusion criteria: • coexisting, severe, chronic debilitating disease • discharge to a nursing home • psychiatric diagnosis • CABG, angioplasty or valve replacement in past 6 months or expected to have such treatment in next 3 months
Interventions	Duration of intervention: up to 10 days after discharge from index admission, on average one week* Intervention: "Supportive educational intervention" During index admission: • intensive education by study nurse using standard nursing care plan After discharge: • study nurse phoned participant within 1 week of discharge to assess potential problems and made appointment for home visit • Home visit on average 1 week after discharge*. At home visit education continued. • If required, study nurse wrote to participant's home care nurse about participant's specific needs • Between discharge and home visit participant could contact study nurse if they encountered problems • After home visit participant encouraged to contact their cardiologist, GP or emergency heart centre with any problems Educational component covered: • symptoms of worsening failure • sodium restriction • fluid balance • compliance and individuals' problems, • included education and support to participant's family Comparison: usual care • "A nurse or physician, depending on his or her individual insight into the patients' questions, provided these patients with education about medication and lifestyle" • Usual care participants did not receive structured education
Outcomes	Primary endpoints: NR

Jaarsma 2000 *(Continued)*

	Measures of QOL: • Heart Failure Functional Status Inventory (to assess functional capabilities at baseline, 3 and 9 months) • symptom occurrence (at baseline, 1, 3 and 9 months), severity and distress questionnaire, designed for this study (at 3 and 9 months) • Psychosocial Adjustment to Illness Scale (at baseline, 3 and 9 months) • Cantril's Ladder of Life (to measure overall well-being at baseline, 1, 3 and 9 months) Measures of self-agency and self-care behaviour: • participants' ability to care for themselves using the Appraisal of Self-care Agency Scale (ASE) (at baseline, 3 and 9 months) • participants' self-care behaviour using a Heart Failure Self-care Behaviour Scale, designed for this study (at baseline, 1, 3 and 9 months) Healthcare resource use: • participants' report of number and reason for contact with GP, cardiologist, medical specialists, physical therapists, social care providers and alternative health specialists • hospital readmissions and outpatient visits from hospital database • reasons for readmission form patient charts Also reported: • deaths at 9 months
Notes	Data source: published data and author contacted for clarification (indicated by *) Funding: "Supported by the Netherlands Heart Foundation, grant 43.033,and Zilveren Kruis, part of Achmea"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "By drawing from an envelope patients were randomly assigned to receive either care-as-usual or the supportive-education intervention".
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The 2 study nurses were involved in data collection as researcher and research assistant. However, the person who collected the data was never the same nurse who visited the patient for the intervention. Health care personnel (cardiologists or staff) involved in the care for the patients did not know if the patient was in the intervention or control group."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Participants themselves knew their assignment, which could have affected self-reported QoL outcome. The 2 study nurses who delivered the intervention were also involved in the study as data collectors and were aware of the allocation status of the participants
Incomplete outcome data (attrition bias) All outcomes	High risk	186 participants enrolled in to the study and 132 (71%) remained at 9 months. 58/84 (69%) remained in the intervention group whilst 74/95 (78%) remained in the control group. Analyses on self-care abilities and behaviour were adjust-

Jaarsma 2000 *(Continued)*

		ed in an attempt to compensate for the influence of attrition - this adjustment assumed that those who dropped out did not improve their self-care and self-agency from baseline this assumption may not have adequately adjusted for attrition.
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Jaarsma 2008

Methods	RCT (17 centres) Recruitment: October 2002-February 2005 Duration of follow-up: 18 months Basic intervention Intervention category: clinic Person delivering the intervention: specialist nurse Intensive intervention Intervention category: case management Person delivering the intervention: multidisciplinary
Participants	Country: Netherlands Total number randomised = 1049 (basic intervention N = 348, intensive intervention N = 353, control N = 348) 26 died before discharge, leaving 1023 in the total group Actual severity of HF in study participants at recruitment: NYHA class, N (%): • basic intervention: class I, N = 0 (0%); class II, N = 171 (51%); class III, N = 159 (47%); class IV, N = 8 (3%) • intensive intervention: class I, N = 0 (0%); class II, N = 165 (48%); class III, N = 163 (48%); class IV, N = 13 (4%); • control: class I, N = 0 (0%); class II, N = 177 (54%); class III, N = 139 (42%); class IV, N = 13 (4%) LVEF: basic: 34 (SD 14); intensive: 33 (SD 15); control: 34 (SD 14) Age: basic: 71 (SD 11); intensive: 70 (SD 12); control: 72 (SD 11) Percentage male: basic: 66; intensive: 61; control: 60 Ethnicity: NR Inclusion criteria: • admitted to hospital with HF NYHA functional class II-IV • aged ≥ 18 years • evidence of structural underlying heart disease as shown at CV imaging • systolic and diastolic dysfunction (preserved LVEF) • stable on standard HF medication before discharge Exclusion criteria: • concurrent inclusion in another study or HF clinic

Jaarsma 2008 *(Continued)*

- inability to complete the questionnaires
- invasive procedure or cardiac surgery intervention performed within the last 6 months
- such procedure or intervention planned to be performed within the next 3 months
- ongoing evaluation for heart transplantation
- inability or unwillingness to give informed consent

Interventions	Duration of intervention: 18 months Intervention: NR Basic intervention: • during index hospital stay: participant (and family) education by HF nurse according to protocol and guidelines, behavioural strategies used to improve adherence • within 2/52 of discharge telephone call to participant from HF nurse • during regular visits to cardiologist at the outpatient clinic (at 2, 6, 12 and 18 months after discharge) additional visits to HF nurse • additional visits just to the HF nurse at the outpatient clinic at one, 3, 9, and 15 months after discharge • telephone access to HF nurse Monday-Friday, office hours, participants (and families) encouraged to contact their nurse if any change in their condition or any questions Intensive intervention: • as for the basic intervention plus: • home visit by HF nurse within 10 days of discharge to assess coping, HF health status general health, and medical, health care and social support. Second home visit 11 months after discharge • weekly telephone calls by the HF nurse in the 1st month after discharge then monthly calls • Out-of-hours back-up to provide 24-h telephone coverage • HF nurse to consult multidisciplinary team at least once during both index admission and once during follow-up to optimise her advice for each participant Control: standard management by cardiologist and, subsequently, GP
Outcomes	Primary (18 months): • time to death (all-cause) or hospitalisation because of HF (composite outcome) • number of days lost to death or hospitalisation • number of readmissions per participant Secondary (18 months): • death from any cause • hospitalisation because of HF • QoL • costs (cost-effectiveness results published by Cao (2013) and Postums (2011))
Notes	Data source: published data only "Financial Disclosure: None reported. Funding/support: This study was supported by grant 2000Z003 from the Netherlands Heart Foundation and by additional unrestricted grants from Biosite France SAS, Jouy-en-Josas, France (brain natriuretic peptide), Roche Diagnostics Nederland BV, Venlo, the Netherlands (N-terminal prohormone brain natriuretic peptide), and Novartis Pharma BV, Arnhem, the Netherlands." Some differences in number of contacts with the cardiologist in all groups: • 40% more cardiologist visits and phone calls in basic group • 10% more cardiologist visits and phone calls in intensive group • 33% more cardiologist visits in control group

Jaarsma 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The computer-generated randomisation scheme used random permuted blocks of 6 patients stratified per centre to ensure balanced assignment of patients to each of the 3 groups in each of the 17 participating centres.”
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "blinded endpoint evaluation"
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	Zero loss to follow-up after intervention started (8 basic group, 9 intensive group, and 9 control participants died before hospital discharge and didn't receive intervention)
Selective reporting (reporting bias)	Unclear risk	Trial retrospectively registered (NCT 98675639) after enrolment complete but before follow-up completed. Costs and QoL mentioned as secondary outcomes, but NR in Jaarsma 2008. Cost evaluation in Cao 2013 and Postums 2011.
Other bias	Low risk	Nothing identified

Kasper 2002

Methods	RCT (2 centres) Recruitment: December 1996-December 1998 Duration of follow-up: 6 months from recruitment (plus additional 3 months) Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: USA Participants: 102 participants (66 men, 65%) in intervention group, 98 (55 men, 56%) in comparison group Actual age of study participants at recruitment: median 63.5 years (range 25-88 years) Male sex: 61% Ethnicity: "white" 64% Actual severity of HF in study participants at baseline NYHA class, N (%): • intervention group: class II, N = 38 (37%); class III, N = 57 (56%) • control: class II, N = 33 (34%); class III, N = 60 (61%) LVEF:

Kasper 2002 *(Continued)*

- intervention group 27.1% (SD 13.8, range 10-70)
- control group mean 27.5% (SD 13.9, range 5-60)

Inclusion criteria:

- admitted to 1 of 2 hospitals with a primary diagnosis of NYHA class III/IV HF
- English speaking.
- Permission from participant's "primary physician"
- judged to be at high risk of HF readmission, i.e. ≥ 1 of the following criteria:
  - aged > 70 years
  - LVEF < 35%
  - ≥ 1 other hospital admission for HF in previous year
  - ischaemic cardiomyopathy
  - peripheral oedema at hospital discharge
  - < 3 kg weight loss while in the hospital
  - PVD
- or any 1 of the following during the index admission:
  - pulmonary capillary wedge pressure > 25 mmHg
  - cardiac index < 2.0 L/min/m2
  - SBP > 180 mmHg
  - DBP > 100 mmHg

Exclusion criteria:

- valvular heart disease requiring surgery
- active substance abuse
- cardiomyopathy (peripartum, hypertrophic with LV outflow tract obstruction or restrictive). Constrictive pericarditis
- psychiatric disease
- dementia likely to limit compliance
- non-cardiac illness likely to cause repeat hospital admission
- heart Tx likely to occur within 6 months
- uncorrected thyroid disease
- serum creatinine ≥ 3.0 mg/dL
- long-term home i/v inotropic therapy
- cardiac surgery or MI during the index admission
- active participation in another research trial
- residence in a nursing home, rehabilitation facility or outside the area served by the 2 hospitals

Interventions	Duration of intervention: 6 months Intervention: "multidisciplinary program" During index hospitalisation: • HF cardiologist designed an individualised treatment plan for each participant before randomisation, which included medication, diet and exercise management After discharge: • "Telephone nurse co-coordinator" phoned participants within 72 h of discharge and then weekly for 1st month, bi-weekly in 2nd month and then monthly. (Content of phone calls: set script with problems pursued as clinically indicated . No medication adjustments over phone.) • Monthly follow-up with HF nurses (usually in HF clinic) • "Primary care physicians" (66% internal medicine physicians, 29% cardiologists) received regular updates from HF nurses and were notified of abnormal lab results.

Kasper 2002 *(Continued)*

- All intervention participants received: pill sorter, list correct medications, list of dietary and exercise recommendations, 24-h telephone contact number and participant educational material
- If required and financial resources limited, participants also received: 3 g sodium 'Meals on Wheels' diet, weigh scale, medications, transport to the clinic and a phone
- HF cardiologist saw participants at 6 months

Content of HF nurse follow-up:

- aimed to implement the treatment plan designed by HF cardiologist by using a pre-specified 55-page algorithm (also designed by the HF cardiologists), which included initiation and titration of drugs, a low sodium diet and exercise recommendations

Comparison group: usual care

- this was care by the participants' primary physicians (73% internal medicine physicians, 26% cardiologists).
- HF cardiologist designed treatment plan for each participant "documented in patient's chart without further intervention"

Outcomes	Primary endpoint (6 months): • total number of HF hospital admissions • all-cause deaths (i.e. composite endpoint) Secondary outcomes (6 months): • death • HF hospital admissions • all-cause hospital admissions • change in HRQOL (MLHFQ) • change in activity status (Duke Activity Status Index) • process indicators including: proportion of participants with systolic dysfunction receiving ACEI according to published guidelines or appropriate alternative treatment if intolerant of ACEI; percentage participants euvolaemic according to defined goal weight; compliance with dietary guidelines using locally developed sodium score and cost data
Notes	Data source: published data and information supplied by study author for 'Rsk of bias' assessments (indicated by*) Funding: "Partial funding was provided by CardioContinuum, Inc., Rockville, Maryland. Under a licensing agreement between The Johns Hopkins University and CardioContinuum, the University and, in particular, its Division of Cardiology, are entitled to royalty on the use of the HF management program described in this study. The University also owns CardioContinuum stock, which is subject to certain restrictions under University policy. The University, in accordance with its conflict of interest policies, is managing the terms of this arrangement. None of the investigators, with the exception of Ms. Van Anden (once an employee of CardioContinuum), have personal stock, royalty interests or consulting arrangements with CardioContinuum."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The coordinating centre made treatment assignments by using an automated telephone response system".
Allocation concealment (selection bias)	Low risk	Quote: "Random number schedules were prepared before initiation of patient recruitment and were unknown to the clinical investigators".

Kasper 2002 *(Continued)*

Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "An independent central telephone data collector, who had no knowledge of the patients' treatment assignment, collected data monthly from all patients during the nine months after enrollment. Medical document coordinators blinded to treatment assignment searched the on-line medical records.... The coordinating center deleted from all documents and records information that revealed personal identity or treatment assignment.... A committee composed of three cardiologists, who had no knowledge of the treatment assignment, categorized each hospital admission and death using documents prepared by the coordinating center."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT principle for main outcomes. QoL data available for 94/102 (92%) intervention and 85/98 (87%) control group at 6 months
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Kimmelstiel 2004

Methods	Multicentre RCT (6 centres) Recruitment period: 22 months, dates NR Duration of follow-up: 12 months Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: USA Number randomised: 200 (control N = 97, intervention N = 103) Actual severity of HF in study participants at baseline NYHA class, %: • intervention: class I, 0%; class II 50.5%; class III 49.5%; class IV 0% • control: class I 1.9%; class II 58.3%; class III 35.9%; class IV 3.9% LVEF: intervention: 30 (SD 14); control: 31 (SD 12) Age: intervention 70.3 (SD 12.2); control: 73.9 (SD 10.7) Percentage male: intervention: 57.7; control: 58.3 Ethnicity: NR Inclusion criteria: • participants were enrolled during an index HF hospitalisation or within 2 weeks of discharge

Kimmelstiel 2004 *(Continued)*

- participants with HF resulting from ischaemic heart disease, dilated cardiomyopathy, valvular heart disease (either surgically treated or deemed inoperable), or hypertensive heart disease

Exclusion criteria:

- noncardiac debilitating illness such as active malignancy
- severe liver disease
- severe renal insufficiency (creatinine 3.0 mg/dL)
- dementia
- obstructive lung disease requiring hospitalisation
- angina at rest or as the principal cause of activity limitation
- MI or revascularisation procedure during the index hospitalisation or within the preceding 30 days
- planned revascularisation or valvular surgery
- restrictive myopathy
- pericardial constriction
- hypertrophic cardiomyopathy

Interventions	Duration of intervention: 90 days, followed by passive surveillance (nurse-manager available for incoming calls but didn't make scheduled calls) for clinically stable participants or continuation for participants with overt clinical instability (class A) Intervention: Specialized Primary and Networked Care in HF (SPAN-CHF) • home visit from nurse-manager within 3 days of discharge, focusing on dietary and medical compliance, daily weights, self-monitoring,and early reporting of changes in weight or clinical status • teaching tool 'Patient and Family Handbook' given to participants during home visit, including sections on HF (definition), medications, low-salt diet, importance of daily weight, and clinical signs and symptoms that should prompt a call to the SPAN-CHF nurse or primary care physician (plus contact phone numbers) • during home visit, nurse performed cardiovascular examination and symptom assessment • Weekly or biweekly phone calls from nurse-manager to participants focused on identifying changes in clinical condition and education reinforcement • participants had 24-h/7-day telephone access to nurse managers, and were instructed to report changes in clinical status and relevant weight change • Frequent communication between nurse-managers, primary care physicians and HF specialist Comparator: usual care
Outcomes	Primary: • hospitalisations for HF during the first 90 days after enrolment Secondary (90 days): • cardiac hospitalisations and all-cause hospitalisations • number of days hospitalised per patient-year of follow-up for HF, cardiac and all-cause hospitalisations at 1 year • costs presented by Gregory 2006, but only for 90-day data not full length of follow-up
Notes	Data source: published data only Funding: "This study was funded in part by grants from the Fannie E. Rippel Foundation and the Hewlett-Packard Corporation."

Risk of bias

Bias	Authors' judgement	Support for judgement

Kimmelstiel 2004 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: "Randomization lists were generated independently for each hospital (in blocks of 4 patients), stratifying patients first by level of care needed."
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Non-nurse study coordinators, blinded to treatment assignment, performed telephone follow-up in all patients at 3 and 12 months after enrolment to ascertain clinical events. Events were adjudicated by an investigator blinded to treatment group."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Subjective outcomes NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Numbers included in analysis NR
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Krumholz 2002

Methods	Single-centre RCT Recruitment period: October 1997-September 1998 Duration of follow-up: 1 year Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: USA Participants: 44 participants (21 men, 48%) in intervention group; 44 participants (29 men, 66%) in comparison group Actual age of study participants: median age 74 years, intervention 75.9 (SD 8.7); control mean age 71.6 (SD 10.3) Male: 57% Ethnicity: "74% Caucasians" Actual severity of HF in study participants at recruitment: Mean EF: intervention group 38% (SD 17); control group 37% (SD 16) NYHA: NR Inclusion criteria: • aged ≥ 50 years • needed to have either admission diagnosis of HF or radiological signs of HF on admission chest X-ray. All participants had been hospitalised for HF • reviewed within 3 days to verify additional set of criteria derived from NHANES-1 Study exclusion criteria:

Krumholz 2002 *(Continued)*

- participants transferred from other hospitals or nursing homes
- participants with HF secondary to high output states or non-cardiac disease
- participants with another terminal illness (e.g. expected survival < 6/12)

Interventions	Duration of intervention: 1 year Intervention: "Education and Support" After discharge: • initial hour-long face-to-face consultation with experienced cardiac nurse within 2 weeks of discharge using a teaching booklet (45% of these consultations took place in participant's home, remainder in hospital clinic) • following this weekly telephone contact for 4 weeks, bi-weekly for 8 weeks then monthly until 1 year • initial consultation covered 5 sequential care domains for chronic illness including: patient knowledge of illness; the relation between medication and illness; the relation between health behaviours and illness; knowledge of early signs and symptoms of decompensation, and where and when to obtain assistance. Follow-up phone calls reinforced the 5 care domains but did not modify current regimens or provide recommendations about treatment. However the nurse could recommend that the participant consulted his/her physician when their condition deteriorated sharply or when they had problems, in order to help participants to understand when and how to seek and access care Comparison: usual care • All usual care treatments and services ordered by their physicians
Outcomes	Primary endpoint: • readmission or death at 12 months' follow-up Secondary endpoints (12 months' follow-up): • all-cause admissions • HF or other CVD-related readmissions • cumulative number of days in hospital • cost of readmission
Notes	Data source: published data and information from author* Funding: "This study was funded in part by grants from the Fannie E. Rippel Foundation and the Hewlett-Packard Corporation."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Computer generated"*
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	"One-year outcomes included deaths, ascertained through next-of-kin, hospital records, active monitoring of obituaries and information about readmissions obtained from patients, their families, discharge summaries and hospital

Krumholz 2002 *(Continued)*

		records to confirm the event and classify the cause, based on the assessment of a clinician blinded to the patients' intervention allocation."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	States ITT analysis used, but numbers included in analysis NR
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	Intervention group significantly older with lower incidence of prior CABG and fewer prescribed calcium channel blockers

Kwok 2008

Methods	RCT (2 centres) Recruitment: September 1999-February 2001 Duration of follow-up: 6 months Intervention category: case management Person delivering the intervention: community nurse
Participants	Country: China (Hong Kong) Number randomised: 105 (intervention N = 49, control N = 56) NYHA: NR LVEF < 40% : 15 (30%) 9 (18%) (intervention, N = 43); (control, N = 50) Age (years): intervention: 79.5 (SD 6.6); control: 76.8 (SD 7.0) Percentage male: intervention: 45; control: 45 Ethnicity: NR Inclusion criteria**:** • hospitalised with a principal diagnosis of HF • age > 60 years • residing within the region and had ≥ 1 hospital admission for HF in the 12 months prior to the index admission. Exclusion criteria: • communication problems but without caregivers • residing in a nursing home • terminal disease with a life expectancy of < six months
Interventions	Duration of intervention: 6 months Intervention: community nurse-supported hospital discharge programme

Kwok 2008 *(Continued)*

	• community nurse (CN) visited participants prior to discharge, to provide health counselling, information on drug compliance, dietary advice • home visit by CN within 7 days of discharge, then weekly for 4 weeks, then monthly, to check vital signs and signs of poorly controlled HF (ankle swelling, dyspnoea and basal crepitation on auscultation). Medications checked and dietary/exercise advice given • home care and day care services arranged if social support insufficient • participants encouraged to contact CN via a telephone hotline during office hours when they developed symptoms • following liaison with geriatrician or cardiologist, CN able to alter medication, arrange appointments and clinical admission as appropriate • CN monitored participants refusing further home visits by telephone Control: usual medical and social care, but with follow-up in the hospital outpatient clinics by the same group of designated geriatricians or cardiologists
Outcomes	Primary: • percentage of participants who ever had unplanned hospital readmissions within 6 calendar months of discharge Secondary (6 months): • number of unplanned hospital readmissions • changes in 6-minute walking test • London Handicap Scale (LHS) domain scores
Notes	Data source: published data only Funding: "The research was funded by the Health Services Research Committee/Health Care & Promotion Fund (HSRC/HCPF) of Hong Kong"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The ward nurses then phoned a second research assistant who assigned trial grouping according to a random number table.”
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: “The research nurse was not aware of the randomisation grouping of the subjects.” Quote: "All hospital admissions, including attendance to the A&E, throughout Hong Kong were traced by an electronic database maintained by the Hospital Authority"
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 1 intervention and 2 control group participants dropped out. Cost analysis based on ITT

Kwok 2008 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Lang 2018

Methods	Single-centre pilot RCT Recruiting: April 2015-June 2016 Duration of follow-up: 6 months Intervention category: case management person delivering intervention: specialist nurse
Participants	Country: Scotland, UK Participants: randomised N = 50 (intervention N = 25; control N = 25) Mean ± SD age: intervention 71.8 (9.9); control 76.0 (6.6) Male sex N (%): intervention 9 (36%); control 14 (56%) Ethnicity: intervention and control both 100% white Actual severity of HF in study participants at recruitment NYHA class: intervention: class I, N = 1 (4%); class II, N = 15 (60%); class III, N = 9 (36%); class IV, N = 0 (0%) Control: class I, N = 1 (4%); class II, N = 16 (64%); class III, N = 8 (32%); class IV, N = 0 (0%) Inclusion criteria: • aged ≥ 18 years • a confirmed diagnosis of HF by EF on echocardiography, radionuclide ventriculography or angiography (i.e., LVEF ≥ 45% within the last 6 months prior to randomisation) Exclusion criteria: • cardiac rehab undertaken within 6 months prior to enrolment • any contraindication to exercise testing or exercise training (with consideration of adapted ESC guidelines for HF)

Interventions	Intervention:
	Participants were provided with:
	• REACH-HF manual, relaxation CD, chair-based exercise DVD, a 'Progress Tracker' tool for patients and a 'Family and Friends Resource' for caregivers
	• participants and caregivers worked through the REACH-HF manual over 12-weeks, facilitated by 2 trained cardiac nurses (at least 1 face-to-face and 2 phone contacts)
	• REACH-HF manual includes:
	  * progressive exercise training programme, tailored to participant's ability and choice of a walking programme or a chair-based exercise DVD, or a combination
	  * managing stress/breathlessness/anxiety.
	  * HF symptom monitoring
	  * taking medication
	  * understanding HF (and why self-management helps).

Lang 2018 *(Continued)*

	The core priorities for caregiver elements of the intervention were: • to facilitate improvement in patient HRQoL by helping them to achieve the core priorities for change • to improve HRQoL for caregivers by acting to maintain their own health and well-being Comparator: usual medical management for HF according to current guidelines
Outcomes	• All-cause mortality • HF readmissions • All-cause readmissions • Serious adverse events • HRQoL (MLHFQ) (EQ-5D and others also reported but not data-extracted as MLHFQ)
Notes	Funding: "National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Grant Reference Number RP-PG-1210-12004). NB, CA, CJG and RST are also supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South West Peninsula at the Royal Devon and Exeter NHS Foundation Trust; KJ by CLAHRC West Midlands and SS by CLAHRC East-Midlands" Study author confirmed majority of participants hospitalised for HF

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote from protocol: "Randomisation numbers will be computer generated and assigned in strict sequence. At the point of randomisation, participants will be assigned the next randomisation number in the sequence. To maintain concealment and minimise selection bias, randomisation will be performed after the baseline visit by a member of Peninsula Clinical Trials Unit (CTU), independent from investigator teams, using a secure, web-based randomisation system."
Allocation concealment (selection bias)	Low risk	Quote from protocol: "To maintain concealment and minimise selection bias, randomisation will be performed after the baseline visit by a member of Peninsula Clinical Trials Unit (CTU), independent from investigator teams, using a secure, web-based randomisation system."
Blinding of participants and personnel (performance bias)	High risk	Quote: "Given the nature of the REACH-HF intervention, it was not possible to blind participants or those involved in the provision of care."
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The statistician undertaking the data analysis was blinded to treatment allocation and we also blinded researchers undertaking collection of outcome data to minimise potential bias. We assessed the fidelity of blinding by asking outcome assessors at each follow-up visit to guess patient group allocation. Unblinding of groups did not take place until after data analysis and the blinded results had been presented to the Trial Management Group and interpretation of results was agreed. "
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL outcomes self-reported by participants not blind to treatment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Losses to follow-up were small and similar between arms (3/25 (12%) in intervention group, 2/25 (8%) in control group, no reasons given)

Lang 2018 *(Continued)*

Selective reporting (reporting bias)	Low risk	Reported outcomes reflect published protocol, although this was published after enrolment began
Other bias	Low risk	Nothing noted

Leventhal 2011

Methods	Single-centre RCT Recruitment: July 2003-February 2005 Duration of follow-up: 1 year Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: Switzerland N randomised = 42, 20 to intervention, 22 to control Age, mean (SD): intervention: 76.7 (7.1); control: 77.6 (6.0) Percentage male: intervention: 59.1 (13%); control: 65.0 (13%) Ethnicity: NR NYHA at discharge: NR Inclusion criteria: • adult patients hospitalised with decompensated HF (NYHA II-IV), irrespective of LVEF • brain natriuretic peptide (BNP) ≥ 100 pg/mL • history of dyspnoea • increased fatigue or weakness • ability to speak German and to comprehend a telephone conversation • discharge to a home setting Exclusion criteria: • acute MI within 8 weeks prior to inclusion • severe myocardial or valvular obstructive disease • uncontrolled angina pectoris • co-morbid conditions compromising prognosis (life expectancy of < 12 months) • planned (except heart Tx) or previous cardiac surgery within 3 months • on dialysis • unstable psychiatric disorders or substance abuse • cognitive impairment (MMSE score < 24) • enrolled in another study • refused to sign an informed consent
Interventions	Intervention: • participant education (HF-educational booklet and kit (Swiss Heart Foundation)) • support with self-care including recognition of warning signs of deterioration • advice on diet, fluids and sodium management • importance of daily weighing

Leventhal 2011 *(Continued)*

- identifying actions to take in case of increasing symptoms, individualised care plans, communication with primary care physician
- Intensity and complexity: intervention duration 12 months, beginning with home visit from specialist HF nurse, followed by 17 structured telephone calls (weekly x 4, bi-monthly x 4, monthly x 6) plus additional calls when needed; 1 call with primary care physician following home visit, additional calls when needed;
- nurse consultation with study internist, study cardiologist or dietician when needed.
- home visit consisted of a physical, psychosocial and environmental assessment, the provision of educational, behavioural, and supportive care to build self-care abilities, and individualised participant goal-setting to increase self-efficacy.
- follow-up telephone calls included discussions of questions or problems the participants had due to their HF identification of signs and symptoms signifying possible decompensation of HF, review of current medications, reinforcement of self-care activities and setting new goals

Comparator:

- all participants received similar care during hospitalisation. This consisted of the normal medical and nursing care provided by hospital staff
- all study participants were examined by the study HF-cardiologist who recommended lifestyle modifications and made suggestions for optimal medical management to the participant's primary care physician
- all participants were given a HF education booklet published by the Swiss Heart Foundation
- these efforts were made to standardise usual care, to remove unnecessary variability in care provided to the control participants
- following hospitalisation, medical care was provided by the primary care physician (usual-care group protocol)

Outcomes	Primary: • mortality (all causes) • readmission (HF related and all causes) Secondary: • QoL (EuroQol- 5D (EQ-5D) and MLHFQ) • length of stay
Notes	Funding: "Funding for this study was provided by the Swiss National Foundation # 3200-068000 (www.snf.ch) and the Swiss Heart Foundation. There are no potential competing interests."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Following discharge, the participant was randomised by an independent centre, according to a computer-generated list (blocked, variable block size)
Allocation concealment (selection bias)	Low risk	The study nurse called the randomisation centre, stated the chronological study recruitment number and was given the group assignment. Participants were notified of their group assignment by telephone
Blinding of participants and personnel (performance bias)	High risk	Quote: "Patients, care-givers, primary care physicians and the intervention nurses were not blinded to group assignment."
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Mortality data were obtained from the Department of Birth and Death Records and re-admission data were obtained from hospital records, exam-

Leventhal 2011 *(Continued)*

		ined and adjudicated by a senior researcher blinded to group assignment, and entered into the database by the study coordinator."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Quote: "Patients were sent the follow-up study questionnaires with a pre-addressed, stamped reply envelope and an appointment for a follow-up telephone interview with a special data collector blinded to group assignments. Questionnaires were entered into the database by research assistants, blinded to group assignment, and checked by random sample by the data analyst." However, participants themselves knew their group assignment, so QoL assessment open to detection bias
Incomplete outcome data (attrition bias) All outcomes	High risk	The trial planned to recruit 300 participants, but the trial was stopped early due to recruitment problems, and only 42 participants were recruited. Kaplan Meier survival analysis was planned to compare time to mortality and time to re-admission. However, since fewer participants were included than was initially planned, preventing calculation of reliable estimates, only a graphical representation of the survival curves were given, without formal testing.
Selective reporting (reporting bias)	Unclear risk	QoL data only reported as a random intercept regression analysis. No protocol found
Other bias	Low risk	Nothing identified

Lopez 2006

Methods	RCT (2 centres) Recruitment: September 2000-August 2002 Duration of follow-up: 1 year Intervention category: case management Person delivering the intervention: pharmacist
Participants	Country: Spain Number randomised: 134 (intervention N = 70; control N = 64) Age: intervention: 75.3 (SD 8.4); control: 76.1 (SD 9.4) Percentage male: intervention: 41.4; control: 46.9 Ethnicity: NR Actual severity of HF in study participants at recruitment NYHA class, N (%): • intervention: class I-II, N = 58 (84.1%); class III-IV, N = 11 (15.9%) • control: class I-II, N = 54 (87.1%); class III-IV, N = 8 (12.9%) LVEF: intervention: 54.5 (SD 14.4); control: 47.4 (SD 17.3) Inclusion criteria: • patients admitted to the General Hospital of Vic and the Municipal Hospital of Badalona for HF who met 2 major or 1 major and 2 minor Framingham criteria Exclusion criteria:

Lopez 2006 *(Continued)*

- regularly living out of the area of influence of the hospital
- regularly living in an old people's home
- moved to a social-health centre or to other centres for acute patients
- suffering any type of dementia or disabling psychiatric disease
- refusing to participate in the study

Interventions	Duration of intervention: 12 months Intervention: Active Information Program, carried out by a pharmacist with 2 key components: • information -personal interview on day of discharge, covering information about the disease, diet education, information on drug therapy and the need for compliance • telephone support - participants given pharmacist's name and phone number, and encouraged to contact about any doubts arising during treatment, or questions about the disease. Monthly during the 1st 6 months and every 2 months thereafter, participants received home phone calls (not clear from whom) to reinforce the intervention and solve any problems or questions arising Comparison: no details given • Follow-up visits at 2, 6 and 12 months to check compliance, QoL and participant satisfaction
Outcomes	Primary (2, 6 and 12 months): • time to the first readmission for HF or for another cause • percentage of participants with readmission • total number of readmissions • total of hospital stay days during the study period Secondary (2, 6 and 12 months): • treatment compliance (NR here) • QoL (EuroQol) • participant satisfaction with the care received and death during the follow-up (NR here)
Notes	Data source: published data only Funding: "This study (PI00/0665) was co-financed with a grant from the Health Research Fund (Fondo de Investigación Sanitaria, FIS) and the European Regional Development Fund (ERDF)." CoI of study authors not provided

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “The patients were randomised to one of the two groups through a randomisation software. Lists were generated in blocks of 4 to assure a consistent patient distribution in both groups.”
Allocation concealment (selection bias)	Low risk	Quote: “Neither the physician nor the nurse responsible for the patient knew the allocation until the educational intervention, the day of discharge”.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information

Lopez 2006 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-reported QoL outcome
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not clear if readmissions reported on an ITT basis. Cost analysis stated to be ITT, but 3 participants were excluded due to missing data on outpatient appointments
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified, although intervention group had slightly higher baseline EF than controls

Mao 2015

Methods	Single-centre RCT Recruiting: June 2010-May 2012 Duration of follow-up: 24 months Intervention category: multidisciplinary Person delivering intervention: multidisciplinary
Participants	Country: Taiwan Participants: randomised N = 349 (intervention N = 174; control N = 175) Mean ± SD age: intervention 59.2 (13.6); control 61.5 (12.6) Male sex, N (%): intervention 127 (73.0); control 117 (66.9) Ethnicity: NR Diabetes, N (%): intervention 66 (37.9); control 82 (46.9) Actual severity of HF in study participants at recruitment: LVEF, mean (SD) %: intervention 36.9 (15.8); control 35.1 (14.3) NYHA class N (%): • intervention: class II, N = 34 (19.5); class III, N = 134 (77.0); class IV, N = 6 (3.4) • control: class II, N = 34 (19.4); class III, N = 130 (74.3); class IV, N = 11 (6.3) Inclusion criteria: • typical signs and symptoms of HF and NYHA functional classification II-IV • hospitalised because of acute cardiogenic pulmonary congestion based on chest X-rays after noncardiogenic causes were excluded • structural abnormalities documented by echocardiograms • aged 20-85 years • both patients with impaired LVEF and those with preserved LVEF were enrolled Exclusion criteria: • having a disorder other than HF that might compromise survival within the next 6 months • bedridden for > 3 months • serum creatinine of ≥ 3 mg/dL

Mao 2015 *(Continued)*

	• dialysis within previous 2 weeks • severe coronary artery disease without complete revascularisation therapy • being pregnant
Interventions	Intervention: • participants were cared for by a HF team consisting of 2 cardiologists specialising in HF care, one psychologist, one dietary assistant, one pharmacist, and 2 case managers (nursing practitioners). Team provided individualised HF education and information on self-monitoring, optimised guideline-based HF medication and complete cardiac and laboratory assessments • 1:1 education sessions with the case manager in hospital; participant diary for daily weight, medication and intake/output; educational booklet (symptoms; importance of monitoring body weight, intake/output; action plans; drug effects and the importance of compliance; diet and exercise • during follow-up: prescheduled outpatient visits to the combined clinic of a cardiologist and case manager 7 days after discharge, then at least monthly or on demand for 6 months (included adjustment of diuretic dose, nutritional consultation, education, drug titration, weighing) • After 6 months, if stabilised, participants visited clinic every 2–3 months, or on demand, with phone contact every month; and 24/7 phone access to case manager Comparator: • primary care cardiologist was responsible for participant evaluation, treatment, and clinic visits (usual care for Taiwan). • neither scheduled follow-up nor specialised HF nurses were provided. • contact with the HF specialists of the research team was discouraged. • participants were advised to contact their primary care cardiologist if they had questions about HF management
Outcomes	• All-cause mortality • HF readmissions
Notes	Funding: National Science Council of Taiwan and Chang Gung Memorial Hospital ClinicalTrials.gov Identifier: NCT01416285. No CoI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer-generated permuted block randomization"
Allocation concealment (selection bias)	Unclear risk	Paper doesn't specify whether block size is concealed or random, so possible to guess assignment of last participant in block
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "A committee of three cardiologists adjudicated all hospitalisations without knowledge of the patients' clinical data to determine whether events were related to worsening heart failure."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Not applicable - QoL NR
Incomplete outcome data (attrition bias)	Low risk	5% of intervention group and 0% of control group lost to follow-up

Mao 2015 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Trials registry states mortality (cardiac and non-cardiac) as an outcome, whereas only all-cause mortality is presented here
Other bias	High risk	Intervention included using guideline-based medications. Post-hoc analysis found that, after adjusting for this, the HR moved closer to the null and there was no evidence for the disease management intervention lowering all-cause death rates

Mehralian 2014

Methods	Single-centre, single-blind RCT Recruiting: September 2011-June 2012 Duration of follow-up: 6 months Intervention category: case management person delivering intervention: nurse
Participants	Country: Iran Participants: randomised N = 110 (intervention N = 55; control N = 55) Mean ± SD age: intervention 61.28 ± 13; control 62.7 ± 10 Male sex: intervention 54%; control 62.2% Ethnicity: NR Actual severity of HF in study participants at recruitment, NYHA class: • intervention - class III most prevalent (67.3%) • control: class III most prevalent (82%) Inclusion criteria: • having HF diagnosed by cardiologist • aged > 18 years • NYHA class II–IV • EF < 45% • ability to read and write Exclusion criteria: • history of other diseases requiring surgery during study period • psychological disorder

Interventions	Intervention: HF education
	• nurses visited participants in their homes, using a checklist:
	  * information about their disease
	  * usual signs and symptoms and potential complications of their illness
	  * prescribed medications
	  * potential change in their lifestyle
	  * special signs and symptoms which they have to know in order to go to the hospital on time
	  * any other information about the illness which participants may request to be answered.

Mehralian 2014 *(Continued)*

	• participants also received a simplified booklet about HF • Home-visits were scheduled twice a month in 1, 3 and 6 months after participants' discharge from hospital • participants and their families were encouraged to make contact in the event of problems Comparator: usual education • provided by nurses 1 h before hospital discharge • nurses visited participants in their room and answered any questions
Outcomes	• All-cause mortality • HRQoL (SF-36 - Iranian version)
Notes	Funding: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "randomly assigned" with no further information
Allocation concealment (selection bias)	Unclear risk	No details given
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Study described as "single blind" but not clear who this applies to - participants were aware of their group assignment due to the nature of the intervention.
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for
Selective reporting (reporting bias)	Unclear risk	No protocol available
Other bias	Unclear risk	More people in the control arm had NYHA class III disease (82% vs 67.3% in intervention group). Not clear whether there were more or fewer people with class IV disease, so possible that disease severity was worse in the control arm.

Mejhert 2004

Methods	Single-centre RCT Recruitment: January 1996-December 1999

Mejhert 2004 *(Continued)*

	Mean (SD) follow-up: 1122 (405) days Intervention category: clinic Person delivering the intervention: nurse
Participants	Country: Sweden Number randomised: 208 (control N = 105, intervention N = 103) NYHA: • intervention: class II, N = 60 (58%); class III, N = 43 (42%); class IV, N = 0 (0%) • control: class II, N = 69 (66%); class III, N = 34 (32%); class IV, N = 2 (2%) LVEF (%): intervention: 34 (SD 12); control: 35 (SD 11), Age: intervention: 75.9 (SD 7.7); control: 75.7 (SD 6.6) Percentage male: intervention: 56; control: 59 Ethnicity: NR Inclusion criteria: • All participants ≥ 60 years of age • hospitalised with HF according to NYHA class II-IV and LV systolic dysfunction by echocardiography Exclusion criteria: • acute MI or unstable angina pectoris within the previous 3 months • valvar stenosis • dementia • severe concomitant disease • refusal to participate
Interventions	Duration of intervention: ≥ 18 months, mean follow-up was 1122 (405) days Intervention: "nurse based outpatient management programme" • regular visits to the outpatient clinic and participant encouraged to keep contact with nurse (not clear how regular) • nurse checking symptoms and signs of HF, blood pressure, heart rate, and weight at each visit • nurses can institute and change medication doses according to standard protocol • participant instructed to check weight regularly and monitor early signs of deterioration • participants with good compliance instructed to change dosing of diuretics on their own • dietary advice recommends restricted sodium, fluid, and alcohol intake • information repeated in booklets and computerised educational programmes Comparator: • treated by GPs according to local health care plan for HF. • all participants had clinical examinations and detailed control of medication at 6, 12, and 18 months at the Cardiovascular Research Laboratory
Outcomes	Primary: • QoL (6, 12 and 18 months) Secondary: • cardiac function (NR?) • medication (6, 12 and 18 months)

Mejhert 2004 *(Continued)*

- hospitalisation (18 months)
- mortality (18 months)

Notes	Data source: published data only Funding: "This study was supported by the Vårdal Foundation, the Swedish Heart and Lung Foundation, the Swedish Society of Medicine, and Karolinska Institutet. " CoI for study authors not provided.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "patients were enrolled and underwent random assignment" but gives no further details on method
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	Appears to report for all participants
Selective reporting (reporting bias)	Unclear risk	Cardiac function stated as a secondary outcome, but doesn't appear to be reported. No protocol found
Other bias	Low risk	No other apparent sources of bias

Naylor 2004

Methods	Multicentre RCT (6 centres) Recruitment: February 1997-January 2001 Follow-up: 1 year Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: USA Participants: number randomised = 239 (control N = 121, intervention N = 118) NYHA:

Naylor 2004 *(Continued)*

- NR

Documented EF, N (%) intervention 88 (72)/control 98 (80)
< 20% 12 (14) / 17 (17) P = 0.755
20 to < 25% 10 (11) / 9 (9) P = 0.760
25 to < 35% 28 (32) / 30 (30) P = 0.914
35 to < 45% 26 (30) / 28 (28) P = 0.942
45% or more: 12 (14) / 14 (14) P = 1.00

Age: intervention: 76.4 (SD 6.9); control: 75.6 (SD 6.5)

Percentage male: intervention: 40; control: 44
Ethnicity: intervention: 66% white; control: 62% white; remainder of participants, African American

Inclusion criteria:

- all patients aged ≥ 65 admitted to study hospitals from their homes February 1997-January 2001 with a diagnosis of HF (diagnosis-related group 127 validated at discharge) were screened for participation
- speak English
- be alert and oriented
- be reachable by telephone after discharge
- reside within a 60-mile radius service area of the admitting hospital

Exclusion criteria:

- end-stage renal disease

Interventions	Duration of intervention: 3 months
	
	Intervention: transitional care delivered by 3 APNs, who received standardised training before the study commenced.
	
	• Quality-Cost Model of APN Transitional Care management strategies, including:
	  * identification of participants' and caregivers' goals
	  * individualised plans of care developed and implemented by APNs in collaboration with participants' physicians
	  * educational and behavioral strategies to address participants' and caregivers learning needs
	  * continuity of care and care co-ordination across settings
	• evidence-based protocol, guided by national HF guidelines, included:
	  * APN discharge planning
	  * initial APN visit within 24 h of index hospital admission, and at least daily during the index hospitalisation for comprehensive assessment of participants and carers
	  * ≥ 8 APN home visits (1 within 24 h of discharge), weekly during the first month then bimonthly during 2nd and 3rd months to check clinical status
	  * additional APN visits based on participants' needs
	  * APN telephone availability 7 days/week (8 am-8 pm, weekdays; 8 am-noon, weekends)
	  * if readmission to hospital required during 1st 3 months, APN resumed home visits
	  * APNs had email/phone access to multidisciplinary team for consultation of cases as required
	  * APNs collaborated with each participants physician regarding adjustments in medications and other therapies or worked under specific guidance from physician
	  * self-management of symptoms was promoted by APNs teaching participants and caregivers about early symptom recognition and effective treatment, such as the use of as-needed diuretics
	  * taped teaching material was left with participants
	
	Comparators:
	
	• routine care (including site-specific discharge planning and clinical paths)
	• standard home agency care if referred, consisting of comprehensive skilled home health services 7 days/week.

Naylor 2004 *(Continued)*

- On-call registered nurse available 24 h/day.
- 58% of control participants received skilled nursing or physical therapy after index discharge

Outcomes	Primary: • time to first readmission or death during 52 weeks Secondary (52 weeks' follow-up): • time to first readmission • total rehospitalisations • QoL • functional status • participant satisfaction • medical costs • cumulative days of rehospitalisation • mean readmission length of stay • number of unscheduled acute care visits after discharge • other treatments and healthcare utilisation • cost of post-index hospitalisation readmission
Notes	Data source: published data only Funding: "The National Institute for Nursing Research, National Institutes of Health funded this study"

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: “research assistants (RAs) blinded to study aims and groups obtained baseline sociodemographic and health status data and notified the project manager, who assigned patients to study groups using a computer-generated, institution-specific block 1:1 randomisation algorithm.”
Allocation concealment (selection bias)	Low risk	As above
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "RAs blinded to study aims and groups conducted standardized patient telephone interviews at 2, 6, 12, 26, and 52 weeks after index hospital discharge to obtain information about rehospitalizations and unscheduled acute care visits to physicians, clinics, and emergency departments; quality of life ...Two cardiologists specializing in the treatment of HF blinded to study group validated reasons for rehospitalizations and categorized them as index related, comorbid (diagnoses abstracted from medical record during index hospitalization), or new health problem."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT principle used, missing QoL data accounted for in analysis (statistical methods described in paper)

Naylor 2004 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Nucifora 2006

Methods	Single-centre RCT Recruitment: March 1999-January 2001 Duration of follow-up: 6 months Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Coutry: Italy Number randomised: 200 (control N = 101, intervention N = 99) NYHA: • intervention: class I, N = 0 (0%); class II, N = 33 (33%); class III, N = 63 (64%); class IV, N = 3 (3%) • control: class I, N = 2 (2%); class II, N = 37 (37%); class III, N = 61 (61%); class IV, N = 1 (1%) LVEF: intervention: 43 (SD 16); control: 43 (SD 19) Age: intervention: 73 (SD 9); control: 73 (SD 8) Percentage male: intervention: 62; control: 62 Ethnicity: NR Inclusion criteria: • Aged ≤ 85 years • admitted to internal medicine department with a diagnosis of HF during recruitment period • HF diagnosed by 2 major or 1 major and 2 minor Framingham criteria Exclusion criteria: • chronic cor pulmonale • terminal illness in addition to HF • severe dementia or other psychiatric illness • indication for surgical therapy in the next 6 months • refusal to participate
Interventions	Duration of intervention: 6 months intervention: "HF management programme" • pre-discharge intensive education by an experienced CV research nurse using a teaching booklet, covering causes of HF, recognition of symptoms of worsening HF, the role of sodium restriction and pharmacological therapy, the importance of fluid and weight control, physical activity and complete abstinence from alcohol and smoking • phone call from nurse 3-5 days post discharge to assess any problems, promote self-management and check compliance, weight and lifestyle issues • participants had telephone access from 8.00 am to 9.00 am, Monday to Friday, and out of hours answering machine

Nucifora 2006 *(Continued)*

	• outpatient visits to doctor at 15 days, 1 and 6 months after discharge, to evaluate test results, physical condition and medicine adherence and make any required changes to drug therapy Control: • pre-existing routine of post-discharge care; i.e. usual care by primary care physician • outpatient visit to doctor at 6 months after discharge
Outcomes	Primary: • all-cause readmissions at 6 months • all-cause deaths at 6 months Secondary (6 months): • event-free survival • days of unplanned readmissions • number of unplanned outpatient visits • participants' clinical status • compliance • adherence to treatment plan • QoL
Notes	Data source: published data only Funding/CoI: NR

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly assigned to receive either the study intervention or the usual care" but gives no details on method of randomisation
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "No patient withdrew from the study. Follow-up data were collected on every patient." However, QoL data at 6 months only available from 74/98 in intervention group and 75/98 in control group
Selective reporting (reporting bias)	Low risk	All stated outcomes reported

Nucifora 2006 *(Continued)*

Other bias	Unclear risk	More participants in the intervention group were in sinus rhythm compared to control group (73% vs 52%, P = 0.06). More participants in control group had previous CABG compared to intervention group (13% vs 5%, P = 0.059)

Ong 2016

Methods	Multicentre RCT (6 centres) Recruiting: October 2011-September 2013 Duration of follow-up: 6 months Intervention category: case management Person delivering intervention: nurse
Participants	Country: USA Participants: randomised N = 1437 (intervention N = 715; control N = 722) Median (IQR) age: intervention 73 (62-84); control 74 (63-82) Male sex: intervention 53.4%; control 52.9% Ethnicity: • intervention: African American 21.5 (18.5-24.5); Hispanic/Latino 12.0; white 54.7; Asian/Pacific Islander or other 11.8 • control: African American 22.7; Hispanic/Latino 10.9; white 54.3; Asian/Pacific Islander or other 12.1 Actual severity of HF in study participants at recruitment: LVEF (%) intervention 42.7; control 43 NYHA class (mean (95% CI) %): • intervention: class I, 0.2 (0.0-0.5); class II, 23.4 (20.0-26.9); class III, 65.6 (61.8-69.4); class IV, 10.8 (8.3-13.3); • control: class I, 0.7 (0.0-1.4); class II, 25.8 (22.2-29.4); class III, 63.9 (59.9-67.8); class IV, 9.6 (7.2-12.0) diabetes: intervention 44.8%; control 47.6% Inclusion criteria: • Individuals admitted as hospital inpatients or on observation status; • ≥ 50 years • receiving active treatment for decompensated HF • expected to be discharged to their home • capable of providing written informed consent in English, Spanish, Farsi, or Russian "Enrollment criteria were expanded in January 2012 to include all patients being actively treated for HF instead of just those having a principal diagnosis of HF. This change was made because patients deemed prospectively as not having a principal diagnosis of HF were being coded as patients with HF after their discharge because of patients with multiple active problems." Exclusion criteria: • transplant recipient/being evaluated/on a waiting list for a transplant • enrolled or enrolling in hospice • expected to expire shortly after discharge • dementia • being admitted from or expected to be discharged to a skilled nursing facility (SNF)

Ong 2016 *(Continued)*

- lack of phone line/reliable cell service
- chronic dialysis
- inability to identify a usual source of care (free clinic acceptable) and who will not be assigned a provider upon discharge.
- Also "patients with the following cardiovascular conditions: patients with valvular disorders requiring surgical intervention (except for those with incidental valvular disease, who will be included), acute myocardial infarction (except for those with demand ischemia, who will be included); patients who are unable to use the intervention equipment (e.g., unable to stand on the weight scale), or who are otherwise unable to comply with the intervention

Interventions	intervention: 3 components conducted by registered nurses: • predischarge HF education by a study nurse, not part of usual care team. Used a booklet and the 'teach-back' method to ensure understanding. Also included demonstration of telemonitoring equipment and the important of monitoring physiological variables • regularly scheduled telephone coaching – 9 calls scheduled over 6 months, usually the same call centre nurse. 1st contact within 2-3 days of discharge to reinforce pre-discharge education, then weekly for the first month. After first month, calls were made monthly until the end of the 6-month study period. Calls were designed to reinforce predischarge education materials • home telemonitoring of weight, blood pressure, heart rate, and symptoms. Results monitored by call centre nurses. Comparator: usual care • "Usual care at the sites included robust pre-discharge education and often a post-discharge follow-up telephone call. No additional surveillance was provided to control patients beyond whatever may have been requested as part of routine clinical practice, and the intervention did not substitute for usual care surveillance. Patients were not precluded from exposure to other readmission reduction or chronic NRs implemented by hospitals, physician groups, or health plans, such as education about HF, pharmacist consultation, and post discharge telephone calls."
Outcomes	• All-cause mortality • All-cause readmissions • HRQoL (MLHFQ)
Notes	Funding: "This study was supported by the Agency for Healthcare Research and Quality; the National Heart, Lung, and Blood Institute (NHLBI); the National Center for Advancing Translational Science, Clinical and Translational Science Institute; the Robert Wood Johnson Foundation; the Sierra Health Foundation; the University of California Center for Health Quality and Innovation; and by the participating institutions. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Block randomization was conducted within each site using random blocks of 4 to 8 individuals via a web-based, computerized, random number generator."
Allocation concealment (selection bias)	Low risk	Web-based implies centralised, and block size was random 4-8
Blinding of participants and personnel (performance bias)	High risk	Not possible due to nature of intervention

Ong 2016 *(Continued)*

Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	States that survey interviews were conducted "by staff at the coordinating center who were unaware of the treatment randomizations"
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	Self-reported QoL
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	There was an unbalanced dropout rate (15% and 26% for intervention and control, respectively, although all randomised participants were included in primary analysis. Hazard models censored data on date of withdrawal for people who had fully withdrawn consent. QoL data only reported for those participants who completed follow-up questionnaire (53.6% and 57.2% for intervention and control, respectively).
Selective reporting (reporting bias)	Low risk	Outcomes match those on clinical trials.gov, posted before trial started
Other bias	Low risk	Outcomes match those on clinical trials.gov, posted before trial started

Rainville 1999

Methods	Single-centre RCT Recruitment: July 1996-June 1997 Duration of follow-up: 12 months Intervention category: case management Person delivering the intervention: pharmacist
Participants	Country: USA Participants: intervention, N = 17 (8 men (47%)); control, N = 17 (9 men (53%)) Actual age of study participants: intervention mean 66.9 (SD 8.7); control mean 72.8 years (SD 10.7) Male sex: 50% Ethnicity: NR Actual severity of HF in study participants at recruitment: NYHA class, N (%): • intervention group class II, N = 1 (6%), class III, N = 12 (71%), class IV, N = 4 (24%) • control group class II, N = 4 (24%), class III, N = 11 (65%), class IV, N = 2 (10%) LVEF: NR Inclusion criteria: • all patients with HF in their admission diagnoses and with a history of HF • age ≥ 50 years Exclusion criteria: • a more significant concomitant disease (e.g. unstable angina, cardiac arrhythmia, COPD) • living in long-term care facility • significant psychiatric illness • long-term renal dialysis • life expectancy < 3 months

Rainville 1999 *(Continued)*

- no home phone
- had a language barrier

Interventions	Duration of intervention: 90 days Intervention: 'pharmacist intervention' During index hospitalisation: • "Routine care plus pharmacist and clinical nurse specialist identified patient issues which posed risk for rehospitalisation and determined corrective action." • before discharge the pharmacist reviewed pathology and treatment of HF, weight monitoring and risk modifications with the participant or caregiver • participant given information brochure, video, weight log and medication organiser • pharmacist also recommended medication changes to physicians After discharge: • pharmacist phoned within 3 days of discharge, and at 7, 30, and 90 days and 12 months to enquire about any readmissions, respond to questions, reinforce information given before discharge • Pharmacist's phone number provided to participants for further support Comparator: usual care • Routine care and preparation for discharge including: written prescription, physician discharge instructions, nurse review of diet, treatment plans and medications; participants provided with computer-generated drug information sheets • At 30, and 90 days and 12 months pharmacist contacted participants to ask about readmissions
Outcomes	Primary endpoint: • hospital readmission for HF or death (composite endpoint) at 1 year
Notes	Data source: published data and information from author* Funding/CoI: no information in paper

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated*
Allocation concealment (selection bias)	Unclear risk	Quote: "Information on patient randomisation was concealed from the patient and all care givers except for the pharmacists involved in the study". It is not clear who was responsible for allocation.
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information in paper
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR

Rainville 1999 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	38 participants randomised, 2 intervention and 1 control participant subsequently excluded as tests during initial hospitalisation showed normal LV function, long-term dialysis was initiated, or participant planned to move out of state after discharge. 1 control participant was lost to follow-up and excluded from analysis.
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

Salehitali 2009

Methods	Single-centre RCT Recruiting: March 1997-March 1998 Duration of follow-up: 6 months Intervention category: case management Person delivering intervention: nurse
Participants	Country: Iran Participants: randomised N = 110 (intervention N = 55, control N = 55) analysed N = 99 (intervention N = 49; control N = 50) Mean ± SD age: NR Male sex (%): intervention 61.2, control 54 Ethnicity: NR Actual severity of HF in study participants at recruitment: NYHA class (%): • intervention: class II, 10.2%; class III, 73.5%; class IV, 16.3% • control: class II, 4%; class III, 82%; class IV, 14% Inclusion criteria: • people with congestive HF Exclusion criteria: • people receiving any surgical intervention • or having any other chronic disease

Interventions	Intervention: an education component and a care component:
	• educational intervention:
	  * education about drugs, type and amount of activity, diet, adverse events (complications) of disease, signs of HF, how to change behaviour and lifestyle
	  * educational needs based on checklist homecare of HF participants, symptoms of return (relapse) of the disease, and immediately referring to the doctor in case of signs and symptoms such as dyspnea, severe swelling, and angina pectoris
	• care intervention:
	  * checking vital signs, weight check, assessing the peripheral swelling
	  * accurate assessment of the amount and timing of drugs

Salehitali 2009 *(Continued)*

	• mode of delivery:
	  * face-to-face education using booklet and CD
	• time of delivery:
	  * interventions delivered when the participants were inpatient in hospital
	  * the interventions continued for 3 more sessions when the participants were at home
	  * to fill the gap between the sessions, there was a phone call following up the interventions
	• timing of interventions:
	  * home care and education interventions were delivered exactly 1 month post-discharge, 2 months after first follow-up, and 3 months after second follow-up
	
	Comparator: usual care

Outcomes	• All-cause readmissions (average per person) • Costs
Notes	Funding: Shahrekord University of Medical Sciences

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"randomised" with no further details
Allocation concealment (selection bias)	Unclear risk	NR
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	NR
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	Not applicable
Incomplete outcome data (attrition bias) All outcomes	Low risk	6/55 intervention group and 5/55 control group dropped out, unclear why
Selective reporting (reporting bias)	Unclear risk	No protocol identified
Other bias	Low risk	Nothing identified

Shively 2013

Methods	RCT, repeated measures Recruiting: September 2006-January 2009 Follow-up: 6 months Intervention category: other

Shively 2013 *(Continued)*

	Person delivering the intervention: nurse
Participants	Country: USA, community setting Participants: N = 43 in intervention group, N = 41 in usual-care group Mean (SD) age: intervention: 63.4 (9.10), usual care: 68.9 (11.73); P = 0.02 Male sex N (%):intervention: 43 (100); usual care: 40 (97.6) Ethnicity: intervention: 33 (76.6%) white; usual care: 32 (78.0%) white Actual severity of HF in study participants at recruitment: NYHA class, N (%): • intervention class I, N = 1 (2.3%), class II, N = 21 (44.2%), class III, N = 23 (53.5%), class IV, N = 0(0%) • control class I, N = 2 (4.9%), class II, N = 18 (48.6%), class III, N = 21 (51.2%), class IV, N = 0 (0%) Median EF%: NR Inclusion criteria: • documented clinical HF stage C • hospitalisation or ED visit for HF treatment within previous 12 months • aged ≥ 18 years • resident in San Diego county • read and speak English • has telephone access • has a primary care provider for routine medical care Exclusion criteria: • inability to provide written consent • acute medical problems within the previous month • considered by the investigators to be medically unstable • enrolled in specialty HF care via the HF Program or telehealth • long-term follow-up by cardiology after a hospital admission as well as severe medical problems • a life expectancy of < 1 year • acute substance abuse or psychiatric problems • homelessness
Interventions	Median duration of intervention: 6 months Intervention: Heart PACT program • the intervention, given by 1 of 2 APNs, used activation theory and was tailored to each participant's activation level, focusing on individualised self-selected goals and moving the participant to a higher level of activation • goals included the importance of self management, improving confidence and knowledge, skills and behaviour goals and plans for these under different situations • each participant met with the intervention nurses for 6 sessions, by telephone or in person. During these meetings, participants' individualised health behaviour goals were discussed, progress toward goals was reinforced, barriers were addressed, and questions were answered • the intervention group received a self-management toolkit (blood pressure cuff, weight scale, pedometer, HF self-management DVD, and educational booklet) at the first intervention visit Comparator: • routine medical care in primary care and specialty clinics (other than the HF Specialty Clinic) at the study site.

Shively 2013 *(Continued)*

- the usual-care group received the self-management toolkit after the final 6-month assessment

Outcomes	Primary outcomes were stated to be: • activation using the Patient Activation Measure (PAM) total score • self-management using the 3 scale scores (maintenance, management, and self-confidence) from the Self-Care of Heart Failure Index (SCHFI) and the Medical Outcomes Study (MOS) Specific Adherence Scale • hospitalizations and ED visits as reported by participants
Notes	Data source: published data only Funding/CoI: NR Generalisability: 263 screened for eligibility, 103 (39%) were eligible, of whom 19 (18%) declined and 84 (82%) enrolled and were randomised to Heart PACT program (N = 43) or usual care (N = 41). 77 assessed at 3 months' follow-up, 68 at 6 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A stratified blocked randomisation approach based on the baseline Patient Activation Measure (PAM) level (low, medium, high) was used to ensure that participants were equally distributed between groups by activation level
Allocation concealment (selection bias)	Unclear risk	No information
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	High risk	Outcome assessors were not blinded to intervention allocation, hospitalisation data reported by participants
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	No QoL data included in review
Incomplete outcome data (attrition bias) All outcomes	Low risk	Statistical analyses assessed missing data as missing at random. Additional analyses used a missing value analyses module using an iterative expectation and maximisation procedure. The additional hypothesis testing analyses using imputed values for missing data are also reported in the paper. 68/84 participants (81%) assessed at follow-up (n NR by group)
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	Participants in the intervention group were younger at baseline (63 vs 69)

Stewart 1999a

Methods	Single-centre RCT Recruiting: March 1997-May 1998 Duration of follow-up: 6 months

Stewart 1999a *(Continued)*

	Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: Australia Participants: intervention, 100 participants (65 men); control, 100 participants (59 men) Actual age of study participants: intervention mean 75.2 years (SD 7.1) years; control mean 76.1 years (SD 9.3) Male sex: 62% Ethnicity: NR Actual severity of HF in study participants at recruitment NYHA class, N: • intervention group class II, N = 42, class III, N = 46, class IV, N = 12 • control group class II, N = 48, class III, N = 43, class IV, N = 9 LVEF: intervention group 37% (SD10); control group mean 37% (SD 11) Inclusion criteria: • Admitted to tertiary care hospital under cardiologist and at least 1previous admission for acute HF (pulmonary congestion or oedema evident on chest X-ray with acute dyspnoea at rest) • NYHA class II-IV • LVEF ≤ 55% • age ≥ 55 years • to be discharged home • lives within hospital catchment area Study exclusion criteria: • terminal disease • valvular disease suitable for surgery • intended heart transplantation • HF precipitated by extensive, reversible ischaemia • home address outside hospital catchment area
Interventions	Duration of intervention: mainly within 2 weeks of discharge but some phone contact throughout study Intervention: usual care plus 'Multidisciplinary, home-based intervention' After discharge: • comprehensive assessment at home by a cardiac nurse 7-14 days after discharge • after home visit nurse sent report to primary care physician and cardiologist • cardiac nurse arranged a flexible diuretic regimen for participant's weight and symptoms if required • phone call by cardiac nurse to participant contact at 3 and 6 months • participants encouraged to contact the nurse if any problems arose • home visits repeated if a participant had ≥ 2 unplanned readmissions within 6 months of index admission Home visit included: • assessment of clinical status, physical activity, adherence to medication, understanding of disease, psychosocial support and use of community resources

Stewart 1999a *(Continued)*

- followed by (as appropriate):
  - "remedial counselling" to participants and their families
  - strategies to improve adherence
  - simple exercise regimen
  - incremental monitoring by family/carers
  - urgent referral to 10 care physicians
- median duration of visit 2 h (range 1-3.5 h)

Comparison Group: usual care

- all study participants could be referred to cardiac rehab nurse, dietician, social worker, pharmacist and community nurse as appropriate
- all participants had appointment with their primary care physician and/or cardiology outpatient service within 2 weeks of discharge.
- regular outpatient review by the cardiologist was undertaken throughout the follow-up period

Outcomes

Primary endpoint (during 6 months follow-up):

- frequency of unplanned readmissions
- all-cause out-of-hospital deaths (i.e. composite endpoint)

Other endpoints (6 months):

- time to first primary endpoint (event-free survival)
- frequency of unplanned readmissions
- days of unplanned readmissions
- all-cause deaths
- out-of-hospital deaths
- cost of hospital and community-based health care (sample of participants only).
- Random sample of participants only: MLHFQ and Australian version of SF-36 at baseline, 3 and 6 months

Notes

Data source: published data only

Funding: NR. CoI: Simon Stewart is a recipient of a National Heart Foundation of Australia Postgraduate Medical Research Scholarship

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Telephone call to an investigator who was unaware of the patient's demographic and clinical profile, who then allocated the individual [to group] via a computer generated protocol."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "all data collection and analysis was done with masking maintained."
Blinding of outcome assessment (detection bias)	High risk	QoL self-reported

Stewart 1999a *(Continued)*

Subjective outcomes		
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Analyses stated to be ITT, but for QoL, quote: "Equal numbers of patients from the intervention and usual-care groups were randomly selected for assessment of changes in health-related quality of life"
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	Quote: "The two groups were well matched for all but number of admissions for acute heart failure and creatinine concentration at hospital discharge."

Stromberg 2003

Methods	Multicentre RCT (3 centres) Recruitment: June 1997-December 1999 Follow-up: 12 months Intervention category: clinic Person delivering the intervention: specialist nurse
Participants	Country: Sweden Number randomised: 106 (intervention N = 52; control N = 54) NYHA: • intervention: class I, N = 0 (0%); class II, N = 7 (13%); class III, N = 39 (75%); class IV, N = 6 (12%) • control: class I, N = 0 (0%); class II, N = 12 (22%); class III, N = 36 (67%); class IV, N = 6 (11%) LVEF: NR Age: intervention: 77 (SD 7); control: 78 (SD 6) Percentage male: intervention: 33/52 (63%); control: 32/54 (59%) Ethnicity: NR Inclusion criteria: • diagnosed HF, either by echocardiography, radiographic evidence of pulmonary congestion or typical symptoms and signs of HF • all participants had been hospitalised for HF Exclusion criteria: • severe chronic pulmonary disease • dementia or other psychiatric illness • short anticipated survival • discharge to a geriatric clinic or home care • already receiving follow-up at the nurse-led HF clinic
Interventions	Duration of intervention: not clear Intervention: nurse-led HF clinic • 1st visit 2-3 weeks after discharge, nurses evaluated status, assessed treatment and provided education about HF and social support

Stromberg 2003 *(Continued)*

- individualised education included both written and verbal information, and was based on guidelines. It included information on HF, treatment, dietary advice, individually adjusted energy intake advice, lifestyle advice (including exercise), and promoted self-management
- nurses contactable by phone during office hours, Monday-Friday, and nurses called participants to provide psychosocial support and evaluate drug changes required
- HF nurses called participants in order to provide psychosocial support, evaluate drug changes or other actions
- extra appointments to attend HF clinic scheduled for participants unstable with symptoms of worsening HF or if further education was needed
- participants referred back to primary health care once they were stable and well informed

Comparator:

- conventional follow-up in primary health care.
- some participants got a scheduled visit after discharge, but most were encouraged to phone primary health care if they had problems due to HF

Outcomes	Primary: • all-cause mortality or all-cause hospital admission after 12 months Secondary (12 months): • mortality due to CV disease or other • number of readmissions for any reason • number of days in hospital • self-care behaviour
Notes	Data source: published data only Funding: Health Research Council in the South-East of Sweden, The Swedish Foundation for Healthcare Science and Allergy Research, The Swedish Heart and Lung Foundation and the Research Foundation of the University Hospital of Linkoping, Sweden. No CoI information given

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomisation was blinded with the use of a computer-generated list of random numbers and sealed envelopes
Allocation concealment (selection bias)	Low risk	As above
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "The assessment and outcome measures were blinded. The nurse doing the assessment and collecting of data was blinded to the intervention and not involved in the care of the patients."
Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR

Stromberg 2003 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	All participants appear to be accounted for, but study authors note that, quote: "The number of readmissions was significantly lower in the intervention group after 3, but not after 12 months. The almost 3 times higher mortality in the control group may have influenced this and we therefore recalculated morbidity data to admissions during time of survival."
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	Quote: “There were significantly more patients with hypertension in the intervention group, 26 vs 16 (p<0.05). There were more patients with diabetes in the control group, 17 vs eight (p=0.05).”

Thompson 2005

Methods	Multicentre, cluster-RCT (2 centres) Recruitment: 20 months, dates NR Follow-up: 6 months Intervention category: clinic Person delivering the intervention: specialist nurse
Participants	Country: UK Number randomised: 106 (intervention N = 58; control N = 48) NYHA: • intervention: class I-II, N = 14 (24%); class III-IV, N = 44 (76%) • control: class I-II, N = 13 (27%); class III-IV; N = 35 (73%) LVEF: intervention: 31 (SD 8); control: 29 (SD 11) Age: intervention: 73 (SD 14); control: 72 (SD 12) Percentage male: intervention: 72; control: 73 Ethnicity: NR Inclusion criteria: • acute admission to hospital with a diagnosis of HF • objective evidence (e.g. echocardiography or coronary angiography) of impaired LVSF as evidenced by a LVEF of at least 45% immediately prior to study recruitment • discharged to home Exclusion criteria: • awaiting an elective cardiac procedure with the intent to reverse the cause of underlying HF (e.g. coronary artery bypass surgery for coronary artery stenosis) • terminal illness other than HF
Interventions	Duration of intervention: 6 months Intervention: "clinic plus home-based intervention" • appointment with specialist nurse prior to discharge, to receive information on HF and medications • office-hours contact number for nurse specialist

Thompson 2005 *(Continued)*

- home visit with 10 days of hospital discharge, for education on symptom management and lifestyle, and clinical examination
- monthly nurse-led outpatient HF clinic for 6 months post-discharge, including education, clinical examination and indices monitoring, and starting of new therapeutic drugs where appropriate

Control group: usual care

- explanation of condition
- prescribed medications by the ward nurse
- referral to appropriate post-discharge support as required).
- participants given an outpatient department appointment 6-8 weeks post discharge

Outcomes	Primary: • event-free survival from either death or recurrent hospitalisation for any reason during the 6-month follow-up Secondary (6 months): • rate of recurrent hospital stay • treatment adherence (NR here) • health-related quality of life
Notes	Data source: published data only Funding: "SS is supported by the National Heart Foundation and theNational Health and Medical Research Council of Australia. This study was supported by a research grant from MerckPharmaceuticals UK."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "a random number allocation was used to allocate equal numbers of small and large clinics to either post discharge HBI+C or UC."
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Data on recurrent hospital stay and/or death were also collated (in a blinded manner) via the local area hospital record system and death registry."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for in primary outcome analysis. High risk of attrition bias for QoL as only 46/106 (overall) participants completed a questionnaire at baseline, and 41 completed it at 6 months
Selective reporting (reporting bias)	Low risk	All stated outcomes reported

Thompson 2005 *(Continued)*

Other bias	Low risk	Quote: "Data on recurrent hospital stay and/or death were also collated (in a blinded manner) via the local area hospital record system and death registry."

Tsuchihashi-Makaya 2013

Methods	Multicentre RCT (3 centres) Recruiting: participants were enrolled from December 2007-March 2010 at 3 cardiology hospitals Follow-up: 12 months Intervention category: case management Person delivering the intervention: specialist nurse
Participants	Country: Japan Participants: N = 161 (intervention, N = 79; usual care, N = 82) Mean ± SD age: intervention, 76.9 ± 10.9; usual care, 75.8 ± 12.1 Male sex N (%): intervention, 42 (53.2); usual care, 49 (59.8) Ethnicity: NR, assumed to be predominantly Japanese Actual severity of HF in study participants at recruitment, NYHA class, N (%): • intervention: class I, N = 8 (10.1%); class II, N = 67 (84.8%); class III, N = 4 (5.1%); class IV, N = 0 • control: class I, N = 14 (17.1%); class II, N = 63 (76.8%); class III, N = 5 (6.1%); class IV, N = 0 Median EF%: NR Inclusion criteria: • hospital admission for HF with symptoms and signs of HF • pre-existing history of chronic HF, NYHA II—IV • ≥ 18 years of age Exclusion criteria: • end-stage HF, defined as requiring mechanical support or continuous i/v inotropic support • a serious life-threatening illness with a life-expectancy of < 6 months • stroke within the last 3 months • cognitive dysfunction • substance abuse or psychotic disorder • participants whose physician or nurses refused access
Interventions	Median duration of intervention: 2 months of home visits, 6 months of phone calls • all enrolled participants received comprehensive discharge education by cardiologist, nurse, dietitian, and pharmacist using a booklet that provided information on pathophysiology, medical treatment, diet, physical activity, lifestyle modification, self-measurement of body weight, self-monitoring of worsening HF, and emergency contact methods. Intervention: home-based disease management programme • a home visit was made within 14 days after discharge from hospital • nurses visited each participant's home to assess how the participant was coping in the home environment, HF status, general health status, adherence to medication, lifestyle modification, daily activity, and social support needs

Tsuchihashi-Makaya 2013 *(Continued)*

- home visits were made once every 2 weeks until 2 months after discharge
- telephone follow-up by nurses in addition to routine follow-up by cardiologists
- at the conclusion of home visiting, nurses conducted monthly telephone follow-up until 6 months after discharge
- nurses monitored HF symptoms, participant's general health status, and requirement for other health and social support
- nurses consulted a multidisciplinary team (cardiologist, dietitian, pharmacist, and social worker) during the intervention period to optimise the advice given to each participant

Comparator: usual care

- comprehensive discharge education as detail above
- after hospital discharge, participants assigned to the usual-care group continued to receive routine management by the cardiologist.
- no extra follow-up by a HF nurse or multidisciplinary team was provided

Outcomes	Primary outcome: • participant's psychological status, including depression and anxiety assessed by HADS secondary outcomes: • QOL (Short Form-8) • all-cause death • hospitalisation for HF (analysed as time to first event; defined as an unplanned overnight stay in a hospital because of progression in HF symptoms or directly related to HF)
Notes	Data source: published data only Funding: "This work is supported by the grants from the Japanese Ministry of Health, Labour and Welfare, the Japan Heart Foundation, and Pfizer Health Research Foundation." CoI: Hiroyuki Tsutsui has received research support from Novartis and honoraria for lectures from Shionogi, Daiichi Sankyo, Tanabe-Mitsubishi, Novartis, MSD, Pfizer, and Takeda."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomized on a 1:1 basis, no further details given
Allocation concealment (selection bias)	Unclear risk	No information given
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Quote: "Prognostic data were reported based on medical records or follow-up by telephone."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	79/84 (94%) intervention group analysed, 82/84 (97.6%) control group analysed. The analysis of primary and secondary endpoints was prespecified

Tsuchihashi-Makaya 2013 *(Continued)*

		to be performed in the per-protocol population, which included all participants who received usual care or home-based intervention, i.e. was not ITT
Selective reporting (reporting bias)	High risk	NCT 01284400 outcomes registered in January 2011, after enrollment ended and 2 months before final data collection. Published protocol (Tsuchihashi-Makaya 2011) states that the secondary endpoint is the time to the first event (all-cause death, cardiac death, sudden cardiac death, or hospitalization for HF). However, Tsuchihashi-Makaya 2013 reports time to first event for all-cause death and hospitalisation (i.e. no mention of cardiac death)
Other bias	Unclear risk	Hospitals were selected on the basis of their organisational capability and enthusiasm for participating in the study. The intervention uses a booklet for the education section and a checklist for follow-up, which could minimise bias if delivered consistently

Tsuyuki 2004

Methods	Multicentre, 2-stage RCT (only 2nd stage randomised) Recruitment dates: September 1999-April 2000 Follow-up: 6 months Intervention category: case management Person delivering the intervention: other
Participants	Country: Canada Number randomised: 276 (intervention N = 140; usual care N = 136) NYHA (%): • intervention: class I, 12%; class II, 48%; class III, 35%; class IV, 5% • control: class I, 14%; class II, 52%); class III, 30%; class IV, 3% Age: intervention: 71 (SD 12); control: 72 (SD 12) Percentage male: intervention: 58; control: 58 Ethnicity: NR Inclusion criteria: • consecutive patients aged > 18 years, admitted to a hospital with a most responsible, primary, secondary, or complicating diagnosis of HF Exclusion criteria: • known secondary causes of HF (i.e. correctable causes as anaemia or hyperthyroidism) • preserved systolic function • were taking an angiotensin-II antagonist because of known intolerance or contraindication to ACE inhibitors • had a terminal illness with a life expectancy < 6 months • cognitive impairment • were unable to communicate because of language barriers • were attending a specialised HF clinic for medical management • were participating in a HF clinical trial • absolute contraindication to ACE inhibitors • participants residing outside the region of the participating hospital

Tsuyuki 2004 *(Continued)*

	• those discharged to a setting where patients were not responsible for own medication administration
Interventions	Duration of intervention: 6 months Intervention: patient support program • 5 key areas: salt and fluid restriction, daily weighing, exercise alternating with rest periods, proper medication use, and early recognition of worsening symptoms • 1-1 education with research co-ordinator prior to discharge using written educational package covering information on HF (definition, causes, symptoms), nondrug treatment, medication information (with special emphasis on proven benefits of therapies), and self-monitoring • adherence aids provided prior to discharge (medication organiser, medication administration schedule, and daily weight log) • participants encouraged to contact co-ordinator for ongoing community support • community follow-up to reinforce education and adherence: telephone contact by the local research co-ordinator at 2 weeks, 4 weeks,and monthly thereafter for up to 6 months post discharge (i.e. 7 calls) • monthly newsletter “Living with Congestive HF”, featuring articles on 5 key components, participant success stories, salt content of foods, low-salt recipes, and compliance tips • research co-ordinator could also recommend that participant consult physician for ACE inhibitor dosage titration as appropriate, or if a problem arose which required further investigation Usual care: • participants received a general heart disease pamphlet before discharge, but no formal counselling beyond routine hospital procedure • monthly telephone contact to check for clinical events
Outcomes	Primary (6 months): • medication adherence, as measured by pharmacy records Secondary (6 months): • clinical events
Notes	Data source: published data only Funding/CoI: "Dr Johnson is a Population Health Investigator with Alberta Heritage Foundation for Medical Research and holds a Canada Research Chair in Diabetes Health Outcomes. Funded by an unrestricted educational grant from Parke Davis Canada (now Pfizer Canada) and the University of Alberta Hospital Foundation."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was conducted by a computer-generated sequence using block randomisation (block size of 4), stratified by study site (hospital).”
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	Quote: "Clinical events, the secondary outcome, were recorded by patient report and through examination of hospital records."

Tsuyuki 2004 *(Continued)*

Blinding of outcome assessment (detection bias) Subjective outcomes	Low risk	QoL NR
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All analyses were by intention to treat"
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	No other apparent sources of bias, although monthly follow-up calls to usual-care group could have provided more contact than would otherwise be expected.

Wierzchowiecki 2006

Methods	Single-centre RCT Recruiting: dates NR Follow-up: 12 months Intervention category: multidisciplinary Person delivering the intervention: multidisciplinary
Participants	Country: Poland; setting: secondary care Participants: N = 160 (intervention, 80 (50%); usual care, 80 (50%)) Mean ± SD age: intervention, 67.3 ± 10.2; usual care, 69.5 ± 10.7 Male sex: 48 (60%) in intervention group, 47 (59%) in control group Ethnicity: NR Actual severity of HF in study participants at recruitment NYHA class, N (%): • intervention group class I, N = 0; class II, N = 13 (16%); class III, N = 35 (44%); class IV, N = 32(40%) • control group class I, N = 0; class II, N = 10 (12.5%); class III, N = 40 (50%); class IV, N = 30 (37.5%) Median EF%: NR Inclusion criteria: • hospitalised patients with HF • established diagnosis • on optimal medical treatment Exclusion criteria: NR
Interventions	Duration of intervention: 12 months Multidisciplinary care: • follow-up 1:1 visits of 30-40 min duration at the HF Clinic (HFC) 14 days and 1, 3, 6, and 12 months post-discharge included consultation with cardiologist, HF nurse, physiotherapist and psychologist. Participants with advanced HF who were unable to come to the clinic were visited at home by HF nurse, visits lasting about 1 h.

Wierzchowiecki 2006 *(Continued)*

- between visits to the clinic, participants were under the care of their primary care physicians. Participants and their GPs could access telephone counselling by HF nurse and cardiologist during working hours
- cardiologist determined underlying disease, reasons for any deterioration, prognostic evaluation and assessment of current treatment, qualifying patients for exercise rehabilitation and psychological referrals
- HF nurse informed participant about multidisciplinary care programme, disease, symptoms, medication side effects and triggers for contact with clinic or emergency care. HF nurse checked adherence to the drug regimen and gave advice about salt, fluids and alcohol intake, sexual activity, necessity of vaccinations, capabilities of a participant to travel or work, etc. He/she also familiarised participant with techniques for blood pressure/BMI measurement etc. and mentioned potential of self-adjustment in drug titration, i.e. furosemide (after telephone call)
- participants received a diary in which to record measurement data and an educational booklet on HF
- participants received education sessions in the form of a lecture from hospital physicians and HF clinic cardiologists, regarding the nature, aetiology, diagnosis and therapy of HF
- physiotherapist, along with cardiologist, set up and monitored the exercise rehabilitation programme
- psychologist presented advice on “how to cope with disease” and performed psychotherapy in participants in whom a high level of trait anxiety was observed (depressive syndrome) by cardiologists.

Comparator: usual care

- participants were cared for by their primary care physicians only
- did not participate in any educational or therapeutic activities

Outcomes	Primary: NR Outcomes: • mortality • rate of rehospitalisation • QoL (MLHFQ) and self-care (the European Heart Failure Self-Care Behaviour Scale)
Notes	Funding: "This Programme was in part financially supported by the Poznań Department of Health and Welfare."

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information in paper
Allocation concealment (selection bias)	Unclear risk	No information in paper
Blinding of participants and personnel (performance bias)	High risk	Not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Unclear risk	No information
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported

Wierzchowiecki 2006 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Low completion rate for QoL questionnaire that was unbalanced between treatment groups (56/80 (70%) in intervention group, 35/80 (43.8%) in usual-care group).
Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Unclear risk	No other issues identified

Yu 2015a

Methods	Single-centre RCT Recruiting: October 2008-January 2010 Duration of follow-up: 9 months Intervention category: case management Person delivering intervention: specialist nurse
Participants	Country: Hong Kong, China Participants: randomised N = 178 (intervention N = 90; control N = 88) Mean ± SD age: intervention 78.6 (7.1); control 78.7 (6.7) Male sex N (%): intervention 59 (53.3); control 32 (36.4) Ethnicity: 100% Chinese Actual severity of HF in study participants at recruitment NYHA class, N (%): • intervention: class II, N = 53 (58.9%); class III, N = 34 (37.8%); class IV, N = 3 (3.3%); • control: class II, N = 50 (56.8%); class III, N = 36 (40.9%); class IV, N = 2 (2.3%) LVEF, mean (SD) %: intervention 41.1 (16.1); control 39.0 (14.3) Diabetes, N (%): intervention 36 (40.0%); control 43 (48.9%) Inclusion criteria: • aged ≥ 60 years • diagnosed with HF according to the Framingham criteria • Chinese • able to communicate • accessible by telephone at home • cognitively intact, as indicated by an Abbreviated Mental Test score (Hong Kong version) of 6 or more out of 10 Exclusion criteria: • discharged to long-term care settings • scheduled for cardiac surgery
Interventions	Intervention: cardiac nurse implemented transitional care model, with: • predischarge visit to assess health status, cultural beliefs, practices of self-care, and post-discharge needs • 2 weekly home visits to assess HF status and self-care implementation at home.

Yu 2015a *(Continued)*

	Customised educational and supportive interventions; • personal self-care goals and action plan to enable effective self-care. • identification of appropriate community care services (including self-help groups, social activities) • phone call 1 week after 2nd home visit, then every 2 weeks for 3 months and then every 2 months for 6 months. Call was to review self-care goal attainment, identify barriers, give relevant advice, and modify action plan accordingly. Cardiac nurse monitored symptom severity and provided prompt advice on self-care decision-making (including when to seek medical consultation). • further home visits offered to participants who had unfulfilled self-care and post-discharge needs • participants had telephone access to cardiac nurse during office hours Comparator: usual care • pharmacy dispensers gave brief instructions when participants collected prescribed medications on hospital discharge. • a regular medical consultation at the specialist clinic was arranged for 4 to 6 weeks after discharge. • no structured educational or supportive postdischarge care was offered
Outcomes	• All-cause mortality • All-cause readmissions • HRQoL (MLHFQ)
Notes	Funding: Hong Kong Jockey Club Charities Trust. No CoI

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Permuted block randomisation (block size = 4, allocation ratio = 1:1), using a computer-generated random number sequence
Allocation concealment (selection bias)	Unclear risk	Computer-generated, but known block size could mean last in block can be predicted.
Blinding of participants and personnel (performance bias)	High risk	Blinding not possible
Blinding of outcome assessment (detection bias) Objective outcomes	Low risk	Quote: "Another research nurse, who had no information about subjects' group status, conducted face-to-face interviews at participants' homes to collect post-test data..."
Blinding of outcome assessment (detection bias) Subjective outcomes	High risk	QoL self-reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Unbalanced dropout (24% usual care, 12% intervention), particular impact on QoL assessment. Main analyses followed ITT principle. For the survival analysis, people lost to follow-up were censored, with no readmission or mortality in the remaining period. Because of an imbalance in dropout rates, 2 sensitivity analyses were conducted: 1) per-protocol (only those who completed intervention and outcome evaluation); 2) worst case scenario analysis – those lost to follow-up assumed to have died or had readmission.

Yu 2015a *(Continued)*

Selective reporting (reporting bias)	Unclear risk	No protocol found
Other bias	Low risk	Nothing identified

ACEI: angiotensin converting enzyme inhibitor; **AP(R)N:** Advanced Practice (Registered) Nurse; **BDI:** Beck Depression Inventory; **BMI:** body mass index; **CABG:** coronary artery bypass graft; **CAS:** Control Attitude Scale; **CoI:** conflicts of interest; **COPD:** chronic obstructive pulmonary disease; **CV:** cardiovascular; **DM:** diabetes mellitus; **DMP:** disease management programme; **ECG:** electrocardiogram; **ED:** Emergency Department; **EF:** ejection fraction; **EHFscBS:** European Heart Failure Self-Care Behaviour Scale; **ESC:** European Society of Cardiology; **GP:** general practitioner; **HADS:** Hospital Anxiety and Depression Scale; **HF:** heart failure; **HRQL:** health related quality of life; **i/v:** intravenous; **IQR:** interquartile range; **ITT:** intention-to-treat; **KCCQ:** Kansas City Cardiomyopathy Questionnaire; **LOS:** length of stay; **LV:** left ventricle; **LVEF:** left ventricular ejection fraction; **LVSF:** left ventricular systolic function; **MI:** myocardial infarction; **MLHFQ:** Minnesota Living with Heart Failure questionnaire; **NIH:** National Institutes of Health; **NIHR:** National Institute for Health Research; **NINR:** National Institute of Nursing Research; **NR:** not reported; **MMSE:** Mini-Mental State Examination; **NYHA:** New York Heat Association functional class; **PAM:** patient activation measure; **PVD:** peripheral vascular disease; **Q:** questionnaire; **QoL:** quality of life; **RCT:** randomised controlled trial; **Rx:** therapy; **SD:** standard deviation; **Tx:** transplantation
*information obtained from personal communication with study author

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
ACTRN12609000442202	Terminated, no results
ACTRN12616000099426	Purely educational intervention
ACTRN12616001627448	Wrong patient population
ACTRN12617001143314	Wrong intervention
Adair 2012	Wrong intervention
Agvall 2013	Hospital admission for HF not an inclusion criterion
Aiken 2006	Not HF disease-specific - participants had HF or COPD (palliative care programme)
Akosah 2002	Non-randomised study
Akosah 2004	Non-randomised study
Al-Mobammad 2015	Wrong study design
Andryukhin 2010	Hospital admission for HF not an inclusion criterion
Angermann 2012	Focus on structured phone-based intervention
Anonymous 2016	Follow-up too short
Artinian 2003	Non-randomised study
Ashton 2014	Wrong study design
Austin 2007	Described as cardiac rehab. Hospital admission for HF not an inclusion criterion
Azad 2008	Hospital admission for HF not an inclusion criterion

Study	Reason for exclusion
Azevedo 2002	Non-randomised study
Balaban 2017	Wrong intervention
Baptiste 2016	Wrong study design
Barth 2001	Very small RCT, limited data presented, statistical analyses appear incorrect
Basoor 2011	Wrong intervention
Bekelman 2014	Wrong comparator
Bekelman 2018	Wrong patient group (hospital admission not an inclusion criterion)
Bell 2016	Wrong follow-up
Benatar 2003	RCT both arms received an intervention
Blaha 2000	Paper discusses methodology of the intervention and is not a study or trial
Bocchi 2004	This reference was identified in an earlier version of this review. We screened the Abstract in this latest update, and found that it did not meet the inclusion criteria, since it is a review of HF clinics in Brazil
Bocchi 2008	Hospital admission for HF not an inclusion criterion
Bondmass 2007	Secondary analysis of data from a previously excluded study
Boutwell 2014	Wrong study design
Bouvy 2003	Hospital admission for HF not an inclusion criterion
Brannstrom 2013	Wrong intervention
Brannstrom 2014	Wrong intervention
Bucci 2003	Hospital admission for HF not an inclusion criterion, and intervention is HF clinic with pharmacy intervention for some
Byrnes 2012	Hospital admission for HF not an inclusion criterion
Capomolla 2004	Wrong intervention
Chen 2017	Wrong study design
Cleland 2005	Pure telemonitoring intervention
Comin-Colet 2016	Wrong intervention
Cordisco 1999	Non-randomised study
Costantini 2001	Mixed before and after and parallel-group study
de la Porte 2007	Hospital admission for HF not an inclusion criterion

Study	Reason for exclusion
de Lusignan 1999	Hospital admission for HF not an inclusion criterion
Deek 2016	Wrong intervention
Deek 2017	Wrong intervention
Delaney 2013	< 6 months' follow-up
Dewalt 2006	Hospital admission for HF not an inclusion criterion
DeWalt 2012	Control arm received a self-management education session, and hospital admission for HF not an inclusion criterion
Dickson 2015	Wrong follow-up
Discher 2003	Non- randomised study
Dracup 2012	Wrong intervention
Dracup 2014	Primarily educational focus
Duffy 2005	Description of development of telephone mediated intervention - no evaluative data
Ekman 1998	< 6 months' follow-up
ElGuindy 2013	Wrong intervention
Evans 1993	"Generic intervention" (i.e. not exclusively designed for, or directed at, peoples with CHF)
Fabbri 2007	Not an RCT. This refers to the DIAL study but is an opinion article on the need for disease management programs in Italy
Farag 1967	Non-randomised study
Feldman 2004	Hospital admission for HF not an inclusion criterion. Nurse-based CRT
Fermann 2017	Wrong participants
Fitzgerald 1994	'Generic' intervention
Flynn 2005	Not an RCT
Foley 2008	Comment on an included study
Fonarow 2004	Editorial
Freund 2011	Wrong patient population
Galbreath 2004	Hospital admission for HF not an inclusion criterion
Gattis 1999	Hospital admission for HF not an inclusion criterion
GESICA 2005	Phone-based
Goldberg 2003	Purely telemonitoring intervention

Study	Reason for exclusion
Goodyer 1995	Hospital admission for HF not an inclusion criterion
Grancelli 2003	Hospital admission for HF not an inclusion criterion
Gregory 2006	Cost data from Kimmelstiel 2004, but only reported in relation to 90-day data so not meeting 6-month minimum follow-up inclusion criterion for this review
Grustam 2015	Wrong intervention
Guder 2015	Wrong study design
Hanchett 1967	Hospital admission for HF not an inclusion criterion
Hancock 2012	Hospital admission for HF not an inclusion criterion
Hansen 1992	'Generic' intervention
Harrison 2002	< 6 months' follow-up
Harter 2016	Wrong participants (confirmed by email with author 16 April 2018)
Haruka 2014	Wrong participants
Heidenreich 1999	Non-randomised study
Heisler 2013	Control cipantss recieved more than usual care
Howlett 2011	Wrong participants
Huffman 2011	Not predominantly people with HF
Huffman 2014	Wrong intervention
Hughes 2000	'Generic' intervention
Hui-Ling 2014	Wrong participants
Inglis 2006	Long-term follow-up of 2 Stewart RCTs, only 1 of which was included in this review. Combined data from the 2 studies presented, so not possible to separate out data from the included and excluded studies
Iraurgui 2007	Primarily educational intervention
ISRCTN18285541	Trial was abandoned for recruitment problems
ISRCTN71548370	Follow-up too short (1 month)
Jaarsma 2003	Methodology paper, no outcome data
Jain 2005	Not an RCT
Jerant 2001	Small RCT with 3 arms: 13 participants receiving home telecare; 12 participants received telephone care; 12 received usual care. An interesting paper but excluded form this review because the presentation and analyses of these data do not allow either of the 2 interventions to be compared with the control treatment.

Study	Reason for exclusion
Johnson 2000	'Generic' intervention
Kakutani 2014	Wrong follow-up
Kalter-Leibovici 2017	Wrong participants (email clarification with study author (1 May 2018) confirmed that data on hospital admission were not collected)
Karhula 2015	Wrong participants
Kato 2013	Purely educational intervention
Khunti 2007	Not all participants had a previous hospital admission for HF
Laramee 2003	< 6 months' follow-up
Ledwidge 2003	Cost study of participants in the excluded study by McDonald 2002
Liljeroos 2017	Wrong participants
Lin 2001	Non-randomised study
Linden 2005	Non-randomised study
Luttik 2009	Comparator not usual care
Luttik 2014	Wrong intervention
Martensson 2005	Hospital admission for HF not an inclusion criterion
Martín-Lesende 2013	Wrong intervention
Matassini 2016	Wrong study design
McClintock 2014	Wrong study design
McCoy 2007	Non-randomised study
McDonald 2002	< 6 months' follow-up
Melin 2014	Wrong follow-up
Menon 2015	Wrong intervention
Moser 2000	Conference poster, no full publication identified at 2012 update. Conference abstract no longer available online, unable to contact study author by email (10 September 2018).
Murray 2007	Hospital admission for HF not an inclusion criterion
Nahlen 2016	Wrong intervention
Naylor 1994	"Generic'" intervention
Naylor 1999	"Generic'" intervention
NCT00202150	Intervention not HF-specific

Study	Reason for exclusion
NCT00300261	Intervention is focussed on telemonitoring
NCT01014884	Intervention not HF-specific
NCT01141907	Intervention is focussed on telemonitoring
NCT01342276	Wrong intervention
NCT01698242	Active control
NCT01820780	Intervention is focussed on medication management
NCT01878630	Intervention is focussed on telecare
NCT01886534	Follow-up too short (3 months)
NCT02110433	Intervention is focussed on telemedicine
NCT02425488	Intervention is educational in focus
NCT03035474	Active control
NCT03220204	Not H- specific
NCT03246035	Follow-up too short (90 days)
NCT03317951	Intervention is focussed on telemonitoring
Nguyen 2007	Hospital admission for HF not an inclusion criterion
O'Riordan 2014	Wrong intervention
Ojeda 2005	Non-randomised study. Contacted study author for clarification, who clarified that this is a non-randomised follow-up of subgroup of participants from the PRICE RCT by Atienza 2004
Oldland 2014	Wrong study design
Oliveira 2017	Wrong follow-up
Otsu 2011	Hospital admission for HF not an inclusion criterion
Palmer 2003	Narrative review
Panella 2005	Not an RCT of the appropriate intervention
Pascual 2011	Generic intervention
Patel 2008	Hospital admission for HF not an inclusion criterion
Pedone 2015	Wrong intervention
Peters-Klimm 2007	Hospital admission for HF not an inclusion criterion
Philbin 2000	Wrong intervention - a quality improvement programme targetted at hospital level

Study	Reason for exclusion
Piamjariyakul 2015	Wrong participants
Powell 2010	No usual-care comparison group Hospital admission for HF not an inclusion criterion
Powers 2014	Wrong follow-up
Quinn 2006	Non-randomised study
Ramachandran 2008	Hospital admission for HF not an inclusion criterion. Contact with study author indicated some may have only been clinic outpatients
Rao 2007	Hospital admission for HF not an inclusion criterion
RBR-9c3ssc	Follow-up too short (90 days)
Reed 2017	Wrong study design
Reeder 2014	Wrong study design
Rich 1993	< 6 months' follow-up
Rich 1995	< 6 months' follow-up
Riegel 2000	Non-randomised study
Riegel 2002	Purely telemonitoring intervention
Riegel 2016	Wrong comparator
Rodriguez-Gazquez 2012	Hospitalisation for HF not an inclusion criterion
Rondinini 2008	Non-randomised study
Rosen 2017	Wrong study design
Rubens 2014	Wrong study design
Rubin 1992	'Generic' intervention
Sanchez 2015	Wrong study design
Santos 2014	Wrong comparator
Scalvini 2016	Wrong intervention
Schneider 1993	Non-randomised study
Schou 2014	Wrong participants
Serxner 1998	Purely educational intervention
Sezgin 2017	Wrong participants
Shepherd 2015	Wrong intervention

Study	Reason for exclusion
Shively 2005	Hospital admission for HF not an inclusion criterion
Sisk 2006	Hospital admission for HF not an inclusion criterion
Smeulders 2006	Hospital admission for HF not an inclusion criterion
Smeulders 2010	Not all participants previously hospitalised for HF
Smith 2005	Hospital admission for HF not an inclusion criterion
Smith 2014	Wrong comparator
Srisuk 2017	Wrong intervention
Stamp 2016	Wrong intervention
Stewart 1998a	'Generic' intervention
Stewart 1998b	Subgroup from a 'generic' study
Stewart 1999b	Subgroup from a 'generic' study
Stewart 2002	Follow-up data at 4.2 years combining data from included study (Stewart 1999a), and excluded study (Stewart 1998a). Data on included study not presented separately
Stewart 2012	Active control arm, not usual care
Stewart 2014	Wrong comparator
TEC4 2016	Wrong intervention
Thompson 2014	Wrong study design
Tibaldi 2009	Active control arm, not usual care
Topp 1998	Non-randomised study
Townsend 1988	'Generic' intervention
Trochu 2003	Not an RCT
Umeda 2014	Wrong intervention
Vaillant-Roussel 2014	Wrong intervention
Valle 2004	< 6 months' follow-up
Van der Kluit 2014	Wrong study design
Van Lieshout 2011	Comparator not usual care
Van Rossum 1993	'Generic' intervention
Villanueva 2015	Wrong intervention

Study	Reason for exclusion
Vorilhon 2016	Wrong intervention
Wagenaar 2015	Wrong intervention
Warber 2011	Not people with CHF
Weinberger 1996	'Generic' intervention
Welsh 2013	Purely educational intervention
Williams 1994	'Generic' intervention
Wongpiriyayothar 2008	Majority of participants had valvular heart disease; not clear if all hospitalised for HF
Woodend 2008	Purely telemonitoring
Yallop 2006	Wrong intervention
Yeshchenko 2014	Wrong intervention
Young 2016	Wrong intervention
Yu 2015b	Wrong follow-up

COPD: chronic obstructive pilmonary disease; **HF:** heart failure; **RCT:** randomised controlled trial

Characteristics of studies awaiting assessment *[ordered by study ID]*

Anguita 2005

Methods	No information
Participants	No information
Interventions	No information
Outcomes	No information
Notes	This is a paper in a Spanish-language journal. It appears to be a cost-benefit analysis of the included study Atienza 2004. We have been unable to find even an abstract to this paper so cannot confirm any characteristics.

Begrambekova 2013

Methods	Prospective randomisation to usual care (N = 249) and to a management programme delivered by doctors/nurse team (N = 288)
Participants	537 participants, included in the National Heart Failure Registry
Interventions	Management programme consists of structured education and follow-up (phone calls)
Outcomes	Primary endpoint

Begrambekova 2013 *(Continued)*

	• NYHA functional class dynamic • QoL outcomes • economic outcomes (particularly: frequency of unplanned readmissions and emergency calls) The mean MLHFQ score at baseline was 57.79 in the active group and 56.96 in the control group. In both groups MLHFQ score significantly decreased at 6 months −11.1; (P < 0.001) and −9,33 (P < 0.001), respectively. The difference between 2 groups was not statistically significant. The HF emergency visits also decreased by 24% (P < 0.001) in active group and by 9.5% (P < 0.015) in control group
Notes	Study author contacted by email 10 April 2018 but no response

Begrambekova 2016

Methods	Secondary analysis of an RCT (Congestive heart failure: a multidisciplinary non-pharmacological approach for changing in re-hospitalisation and prognosis in patients (CHANCE))
Participants	745 people with HF and depressive symptoms
Interventions	Disease management programme • structured education • regular follow-up (phone calls)
Outcomes	• Russian version of HADS • Composite of CV mortality and HF readmission
Notes	Study author contacted by email for further details of CHANCE trial 10 April 2018 but no response Linked conference abstract (Mareev 2010) is for the CHANCE-AND trial, but also mentions the CHANCE trial. Study author not traceable

Chung 2014

Methods	RCT of 24 patient-caregiver dyads
Participants	24 people with HF and their family caregivers
Interventions	Family cognitive education therapy • CBT • educational self-care intervention
Outcomes	• Depression (Patient Health Questionnaire) • QoL (MLHFQ) at 6 months
Notes	Study author contacted by email 23 April 2018 to clarify whether majority of participants had been admitted to hospital for HF, and whether the intervention was tailored to HF or a 'generic' intervention. No response

Fan 2010

Methods	Not clear from abstract - "divided into groups"
Participants	145 hospitalised patients with HF
Interventions	Education for participants: • diets • self-management • surveillance of HF symptoms • explanation of drugs or devices used for HF. Follow-up phone calls for participants in stable condition: • phone calls every 4 weeks. Follow-up phone calls for participants in unstable condition: • phone calls every week. Visits to the heart clinic to see specialists who major in HF provided treatment: • adjustment of drug doses • change of drugs • health consultation for participants and their family members
Outcomes	• NYHA functional class • LVEF • Self-monitoring indicators • Achievement of target doses of beta-blockers • CV event rate
Notes	We assessed this Chinese-language study as potentially meeting the inclusion criteria, but we have been unable to get a data extraction done for this review

ISRCTN13668364

Methods	Cluster-RCT
Participants	People with HF
Interventions	Specialised nurse clinic (intervention) versus conventional HF treatment (control)
Outcomes	• ECHO utilisation • Angiotensin convertin enzyme-inhibitor use • Readmission rates
Notes	Recruitment status: completed. Enrollment started in 2000, but no results or publications identified

Mizukawa 2014

Methods	Multicentre RCT (pilot study), January 2013-April 2014

Mizukawa 2014 *(Continued)*

Participants	59 people with HF

Interventions	3 arms:
	• tele-monitoring group
	  * participants had a device to measure noninvasive blood pressure, heart rate, body weight measurements that automatically sent data to the monitor centre
	  * nurses gave participants teleconsultation when the data were out of the optimal values
	  * participants also received a disease management programme to gain self-management skills
	• disease management programme
	  * participants write the value of blood pressure, heart rate, and body weight to monitor their conditions.
	• usual-care group
	  * standard self-management education once from a nurse
	  * participants visited the physicians as usual

Outcomes	• Readmission for HF
Notes	Emailed only traceable study author (toshirok@hiroshima-u.ac.jp) on 1 May 2018 to ask for further details on whether hospitalisation for HF was an inclusion criterion and whether results published in full, but no response

NCT00166049

Methods	Factorial RCT
Participants	HF
Interventions	3 arms: • patient family education (intervention 1) • family partnership intervention (intervention 2) • usual care (control)
Outcomes	Primary: • adherence to dietary sodium and medication-taking behaviour • physical status • psychological status • HRQoL Secondary: • health resource utilisation • autonomy support • perceived family criticism • knowledge
Notes	Recruitment status: completed. Study completion date: May 2011. No results found

NCT00182182

Methods	Cluster -RCT
Participants	HF
Interventions	Primary case-based disease management strategy
Outcomes	Primary: • process-of-care composite score, • ACEI-inhibitor use Secondary: • disease-specific QoL, • NYHA functional class • all-cause hospitalisation • HF hospitalisation • ED visits for HF • referral to HF clinic • quality-adjusted survival • overall costs
Notes	Recruitment status: unknown. Study completion date was October 2006. No results found and comparator unclear

NCT01378247

Methods	RCT
Participants	Adults with HF
Interventions	Family-focused nursing vs treatment as usual
Outcomes	Primary: • HRQoL Secondary: • change in European Heart Failure Self-Care Behavior Scale • change in Family Functioning, Health and Social Support Scale • change in Self-Efficacy for Managing Chronic Disease 6-item scale • change in Major Depression Inventory diagnostic scale • re-admissions • HF re-admissions • mortality
Notes	Recruitment status: completed. Study completion date: January 2017. No results published/posted

NCT01461681

Methods	RCT

NCT01461681 *(Continued)*

Participants	Adults with HF
Interventions	Symptom management service for HF versus usual cardiology care
Outcomes	Primary: • change in depression assessed at baseline, 3 months and 6 months Secondary outcomes: NR
Notes	Recruitment status: completed. Study completion date: December 2013. No results published/posted

NCT02112227 PACT-HF

Methods	Cluster-RCT
Participants	Adults and children (≥ 16 years) with HF
Interventions	Discharge planning services versus standard care
Outcomes	Primary: • time to composite of all-cause readmissions • emergency department visits • death at 30 days and 3 months Secondary: • preparedness for discharge • QoL on admission, at 6 weeks and 6 months post-discharge • healthcare costs
Notes	Recruitment status: completed. Study completion date: June 2016. No results published/posted

NCT02251899

Methods	RCT: "A disease management study targeted to reduce health care utilization for patients with congestive heart failure". Start date January 2010, estimated study completion date June 2016
Participants	Estimated enrolment: 10,000 adults with ≥ 1 unplanned inpatient occasion with primary diagnosis of HF during the last 12 months
Interventions	Disease management intervention (DMI): • nurse-managed • regularly delivered by telephone or, when necessary, in person Control - not receiving the DMI
Outcomes	Primary outcomes (at 2 years) • number of hospitalisations • number of outpatient visits to medical doctor

NCT02251899 *(Continued)*

	Secondary outcomes (at 2 years) • mortality • length of hospital stays • total health care cost
Notes	Gustaf Edgren (gustaf@pheph.se) contacted 16 April 2018 to see if any results are available yet - no response

NCT02331524

Methods	3-arm RCT
Participants	Adults > 40 years with HF
Interventions	• Feedback with associated encouragement about daily activity (intervention 1) • Health coaching with associated individualised home exercise programme (intervention 2) • Usual care (control)
Outcomes	Primary: • change in Medtronic implanted device patient activity measure Secondary: • ActiGraph daily activity • 6-min walk test • 30 seconds timed chair rise • QoL • health care utilisation
Notes	Recruitment status: completed. Study completion date: July 2016. No results published/posted

Ortiz 2017

Methods	RCT 2011-2013, patients were prospectively randomly allocated (1: 2) to standard care or intervention
Participants	127 patients with reduced EF
Interventions	• Nurse-led clinic cross intervention programme (health education and drug treatment optimisation) • Standard care
Outcomes	Primary composite endpoint • mortality and hospital readmissions from any cause. Secondary endpoints • all-cause mortality • all-cause hospital readmissions • HF readmissions

Ortiz 2017 *(Continued)*

	• time to 1st admission • QoL improvements (assessed by MLHFQ)
Notes	Emailed study author for clarification of whether majority of participants had been admitted to hospital for HF (1 May 2018). No response

Shao 2014

Methods	RCT
Participants	120 HF outpatients in the medical centre
Interventions	Self-management intervention. "Diet control" strategy focused on sodium and fluid restriction: • appraisal • goal setting • self-monitoring of diet control, symptoms and daily weight. Comparison • did not receive this intervention
Outcomes	• Self-efficacy for salt and fluid control • HF self-management behavior • HF symptoms • Depressive symptoms • Daily weight monitoring • HF health services utilisation
Notes	Emailed study author (1 May 2018) for clarification of whether majority of participants had been admitted to hospital for HF, and whether the conference abstract was now published as a full paper. No response

ACEI: angiotensin converting enzyme inhibitor; **CV:** cardiovascular; **ED:** Emergency Department; **EF:** ejection fraction; **HADS:** Hospital Anxiety and Depression Scale; **HRQoL:** health-related quality of life; **MLHFQ:** Minnesota Living with Heart Failure questionnaire; **NYHA:** New York Heart Association; **QoL:** quality of life; **RCT:** randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Bendelac 2014

Trial name or title	OSICAT
Methods	Prospective, multicentre RCT
Participants	People with chronic HF
Interventions	Ttelecardiology programme: • daily scale assessment • a device asking the participants daily questions on the symptoms associated with their HF • regular telephone calls made by nurses

Bendelac 2014 *(Continued)*

Outcomes	• All-cause mortality assessed at 6, 12 and 18 months • Hospitalisation assessed at 6, 12 and 18 months • Cost-utility study: the economic analysis will adopt the healthcare payer's perspective and will take into account direct costs, indirect costs and informal care costs. • Social and organisational acceptability
Starting date	2014
Contact information	Pro Galinier: galinier.m@chu-toulouse.fr
Notes	Contact with Prof Galinier (16 April 2018) confirmed that this study has not yet been completed.

Ding 2017

Trial name or title	Innovative telemonitoring enhanced care programme for chronic heart failure (ITEC-CHF) to improve guideline compliance and collaborative care: protocol of a multicentre randomised controlled trial
Methods	Mutlicentre RCT
Participants	300 people with chronic HF

Interventions	Innovative telemonitoring enhanced care programme for HF (ITEC-CHF)
	• usual care
	• additional telemonitoring service
	  * remote weight monitoring
	  * structured telephone support
	  * nurse-led collaborative care
	Comparator:
	• usual care

Outcomes	Primary outcomes: • compliance rates with the best-practice guidelines for daily weight monitoring Secondary outcomes: • compliance with other guideline recommendations (health maintenance, medication, diet and exercise), • health (HRQoL, risk factors, functional capacity and psychological states) • economic outcomes related to the use of healthcare resources such as hospital readmissions and GP/ED visits
Starting date	Recruitment started 20 January 2015, anticipated last enrolment was 31 March 2017
Contact information	Trial registration number: registered with Australian New Zealand Clinical Trial Registry (ACTRN12614000916640). Hang.Ding@csiro.au
Notes	Email contact with study author (31 May 2018) confirmed that the trial is complete but the results paper is being drafted so results not yet available

Hardman S

Trial name or title	The evaluation of a nurse-led intervention to improve self-management for patients admitted to hospital with a diagnosis of heart failure (due to left ventricular systolic dysfunction)
Methods	RCT
Participants	250 participants (125 in intervention arm, 125 in control arm)
Interventions	The intervention is designed to enhance participants' sense of self efficacy (confidence) in their ability to adhere to medication and other aspects of their treatment regime including: • fluid restriction • diet • exercise • self-monitoring for signs of deteriorating HF • using a problem-solving approach
Outcomes	Primary endpoints during 1st 3 months after discharge: • all-cause hospital readmissions • HF hospital readmissions Numerous secondary endpoints including mortality and 12-month data.
Starting date	NA, study likely to be completed in 2005
Contact information	Dr. Suzanna Hardman Consultant Cardiologist with an interest in Community Cardiology, The Whittington & UCL Hospitals, Clinical & Academic Department of Cardiovascular Medicine, St Mary's Wing, Whittington Hospital, Highgate Hill, London N19 5NF, UK.
Notes	Contacted study author July 2010, publication expected soon. Contacted 11 September 2018 for further update as no publications identified, no update

Massie 2001

Trial name or title	A controlled trial of heart failure management programs
Methods	Controlled trial
Participants	147 patients with symptomatic HF at 5 VA facilities
Interventions	3 groups: • usual care • nurse manager • home monitoring Also in two sites patients randomised to HF clinic
Outcomes	Death or hospitalisation for a cardiac cause
Starting date	NA
Contact information	NA

Massie 2001 *(Continued)*

Notes	Poster abstract only. Study author contacted, full trial not published. No further publications identified

NCT02044211

Trial name or title	Blended collaborative care for heart failure and co-morbid depression
Methods	RCT
Participants	HF and depression
Interventions	• Collaborative care for HF and depression (intervention 1) • Collaborative care for HF only (intervention 2) • Usual care for HF and depression (control)
Outcomes	Primary: • mental HRQoL Secondary: • HF-related QoL • mood symptoms • rehospitalisation • mortality (all-cause and cardiovascular) • costs • employment
Starting date	February 2014
Contact information	Principal Investigator: Bruce L. Rollman, University of Pittsburgh
Notes	Estimated study completion date: June 2019.

NCT02481921

Trial name or title	MEDIC-HF
Methods	RCT
Participants	Adults with HF
Interventions	• Group medical visits • Usual care
Outcomes	Primary: • QoL Secondary: • time to hospitalisation or death

NCT02481921 *(Continued)*

Starting date	1 June 2015
Contact information	Contact: Wen-Chih H Wu (wen-chih.wu@va.gov), Tracey Taveira (tracey.taveira@va.gov)
Notes	Recruitment status: recruiting

NCT02894502

Trial name or title	MOTIVATE-HF
Methods	RCT
Participants	Adults with HF
Interventions	• Motivational interviewing only for participants (intervention 1) • Motivational interviewing for participants and caregivers (intervention 2) • No intervention (control)
Outcomes	Primary: • self-care in participants and care-givers Secondary: • burden of HF symptoms • QoL • participant hospitalisation • use of emergency services • death
Starting date	June 2014
Contact information	Contact: Ercole Vellone (ercole.vellone@uniroma2.it), Rosaria Alvaro (rosaria.alvaro@uniroma2.it)
Notes	Estimated study completion date: December 2018

NCT03012256

Trial name or title	DIVERT-CARE
Methods	RCT
Participants	Adults ≥ 19 years with HF and COPD
Interventions	• Cardio-respiratory management model • Standard care
Outcomes	Primary: • first unplanned ED visit • total care costs • changes in participant activation

NCT03012256 *(Continued)*

	• number of symptoms Secondary: • number of unplanned ED visits • HRQoL Follow-up: 6 months
Starting date	6 February 2018
Contact information	Contact: Andrew Costa (acosta@mcmaster.ca), Graham Campbell (campbg4@mcmaster.ca)
Notes	Recruitment status: recruiting. Estimated study completion date: December 2019

NCT03035123

Trial name or title	EduStra-HF
Methods	RCT
Participants	HF
Interventions	• Therapeutic education • Usual care
Outcomes	Primary: • number of rehospitalisations for acute HF Secondary: • participants' knowledge about illness • QoL • length of stay for HF and all-cause hospitalisations • hospitalisation rate for CVDs except HF • CV and all-cause mortality rate, • BNP or NT pro-BNP levels Other: • cost-effectiveness Follow-up: 1 year
Starting date	1 April 2017
Contact information	
Notes	Estimated study completion date: 30 June 2020

NCT03108235

Trial name or title	HOM-HEMP

NCT03108235 *(Continued)*

Methods	RCT
Participants	Adults ≥ 55 years with chronic HF
Interventions	• Home-based self-management psychosocial educational programme (HOM-HEMP) (intervention 1) • HOM-HEMP with smartphone app (intervention 2) • Standard care (control)
Outcomes	Primary: • cardiac self-efficacy scale Secondary: • HADS, • HRQoL • Social Support Questionnaire • Self-Care Heart Failure Index Other: • 6-minute walk test • NYHA functional class • LVEF • unplanned health services use • process evaluation
Starting date	1 January 2018
Contact information	Contact: Wenru Wang (nurww@nus.edu.sg)
Notes	Estimated study completion date: 30 December 2019

NCT03555318

Trial name or title	Intervention by a cardiologist and geriatrician in elderly patients after admission due to heart failure
Methods	RCT
Participants	Patients > 75 years with a recent admission for HF (within the previous 10 days)
Interventions	Intervention: • participants randomised to a combined ambulatory follow-up with a cardiologist and a geriatrician Comparator: • participants randomised to usual care (ambulatory follow-up with a cardiologist)
Outcomes	Primary: • all-cause hospitalisation Secondary:

NCT03555318 *(Continued)*

	• HF hospitalisation • QoL • functional capacity • medication use • number of outpatient visits • ED visits • hospitalisations
Starting date	Not yet recruiting (as of June 13, 2018) Estimated study completion is June 14, 2020
Contact information	Nuria Farre, NFarreLopez@parcdesalutmar.cat
Notes	

Oksman 2017

Trial name or title	TERVA: Tele-based health coaching program for chronic disease in primary care (NCT00552903)
Methods	RCT
Participants	1570 patients with type 2 diabetes, coronary artery disease or congestive HF
Interventions	Intervention: • monthly individual health coaching by telephone from a specially trained nurse for 12- months • routine social and healthcare Control: • routine social and health care
Outcomes	• HRQoL (15D instrument to measure utility) • Cost-effectiveness ratios (ICER, QALY)
Starting date	Unclear
Contact information	NCT00552903 Kristiina Patja <kristiina.patja@promedico.fi>
Notes	Contact with study author (14 May 2018) indicated that the full 8-year clinical outcome data are not yet published or available for this study, nor the relevant clinical outcome data for the Patja 2012 reference. The Oksman 2017 paper contains cost-effectiveness data and a measure of health utility.

Pugh 1999

Trial name or title	Nursing case management for elderly heart failure patients
Methods	Not clear
Participants	200 patients aged ≥ 65 years hospitalised at 1 centre for the treatment of HF
Interventions	Intervention: • enhanced discharge planning

Pugh 1999 *(Continued)*

	• taught to manage their HF within parameters set by their physician using a workbook for guidance • receive participant-specific printed material • ongoing assessment and follow-up by a nurse for a 6-month period through phone calls and visits
Outcomes	• Morbidity • Mortality • QoL • Functional status At 6 months and 1 year after discharge
Starting date	NA, in July 1998 57 participants had been recruited
Contact information	NA
Notes	No publications identified

Taylor 2015

Trial name or title	Rehabilitation Enablement in Chronic Heart Failure (REACH-HF) facilitated self-care rehabilitation intervention in heart failure patients and caregivers
Methods	Multicentre, parallel, 2-group RCT
Participants	216 patients with systolic HF and their caregivers
Interventions	Intervention: • self-help manual delivered by specially trained facilitators over a 12-week period • usual care Control • usual care alone (control)
Outcomes	Primary: • participants' disease-specific HRQoL (MLHFQ) at 12 months' follow-up. Secondary: • survival • HF hospitalisation • blood biomarkers • psychological well-being • exercise capacity • physical activity • other measures of QoL • participant safety and QoL • psychological well-being • perceived burden of caregivers at 4, 6 and 12 months' follow-up. A cost-effectiveness evaluation will also be carried out.
Starting date	13 November 2014

Taylor 2015 *(Continued)*

Contact information	Trial registration number: ISRCTN86234930 r.taylor@exeter.ac.uk
Notes	Pilot paper by Greaves 2016 does not contain outcomes relevant to this review. Full publication expected soon

Vellone 2017

Trial name or title	MOTIVATE-HF; NCT02894502
Methods	3-arm, multicentre RCT
Participants	240 people with HF and their caregivers
Interventions	Motivational interviewing; 3 arms: • motivational interviewing intervention to only participants • motivational interviewing intervention to participants and caregivers • standard care to participants and caregivers
Outcomes	• Self-care maintenance; self-care management, self-care confidence, • HF somatic symptom perception • Generic and disease-specific QoL • Anxiety and depression • Cognition • Sleep quality • Mutuality with caregiver • Hospitalisations • Use of emergency services • Mortality
Starting date	June 2014, estimated study completion date December 2018
Contact information	ercole.vellone@uniroma2.it
Notes	Email from study author (1 May 2018) confirmed that data collection is now complete but the main article is not yet ready for dissemination.

COPD: chronic obstructive pulmonary disease;**CV:** cardiovascular; **CVD:** cardiovascular disease; **ED:** Emergency Department; **GP: G**eneral Practitioner; **HADS:** Hospital Anxiety and Depression Scale; **HF:** heart failure; **HRQoL:** health-related quality of life; **ICER:** incremental cost effectiveness ratio **LVEF:** left ventricular ejection fraction; **NYHA:** New York Heart Association; **QALY:** quality-adjusted life year; **RCT:** randomised controlled trial

DATA AND ANALYSES

Comparison 1. Case management vs usual care

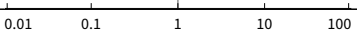
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All-cause mortality - main analysis	26	6903	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.68, 0.90]
2 All-cause mortality - subgroup analysis by length of follow-up	26	6903	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.68, 0.90]
2.1 6 months' follow-up	10	3253	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.70, 1.11]
2.2 More than 6 months' follow-up	16	3650	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.62, 0.88]
3 All-cause mortality - subgroup analysis by person delivering the intervention	26	6903	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.68, 0.90]
3.1 Specialist nurse	13	2268	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.61, 1.01]
3.2 Nurse/community nurse	6	2645	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.69, 1.03]
3.3 Pharmacist/community pharmacist	3	507	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.25, 1.67]
3.4 Multidisciplinary	2	869	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.50, 1.03]
3.5 Other	2	614	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.42, 1.71]
4 All-cause mortality - sensitivity analysis with low risk of bias	10	3514	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.55, 0.82]
5 HF readmissions - main analysis	12	2528	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.53, 0.78]
6 HF readmissions - subgroup analysis by length of follow-up	12	2528	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.53, 0.78]
6.1 6 months' follow-up	4	778	Risk Ratio (M-H, Random, 95% CI)	0.72 [0.58, 0.88]
6.2 More than 6 months' follow-up	8	1750	Risk Ratio (M-H, Random, 95% CI)	0.60 [0.45, 0.81]
7 HF readmissions - subgroup analysis by person delivering the intervention	12	2528	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.53, 0.78]
7.1 Specialist nurse	7	945	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.47, 0.70]
7.2 Nurse/community nurse	1	252	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.42, 1.16]
7.3 Pharmacist/community pharmacist	1	34	Risk Ratio (M-H, Random, 95% CI)	0.4 [0.16, 1.03]
7.4 Multidisciplinary	1	683	Risk Ratio (M-H, Random, 95% CI)	1.08 [0.84, 1.39]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.5 Other	2	614	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.45, 0.88]
8 HF readmissions - sensitivity analysis with low risk of bias	4	741	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.50, 0.77]
9 All-cause readmissions - main analysis	14	4539	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.83, 1.01]
10 All-cause readmissions - subgroup analysis by length of follow-up	14	4539	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.83, 1.01]
10.1 6 months' follow-up	5	2120	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.89, 1.11]
10.2 More than 6 months' follow-up	9	2419	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.78, 1.01]
11 All-cause readmissions - subgroup analysis by person delivering the intervention	14	4539	Risk Ratio (M-H, Random, 95% CI)	0.92 [0.83, 1.01]
11.1 Specialist nurse	6	853	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.73, 0.99]
11.2 Nurse/community nurse	4	2255	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.92, 1.09]
11.3 Pharmacist/community pharmacist	1	134	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.45, 1.03]
11.4 Multidisciplinary	1	683	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.92, 1.21]
11.5 Other	2	614	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.57, 1.38]
12 All-cause readmissions - sensitivity analysis with low risk of bias	6	2217	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.74, 1.02]
13 Quality of life (MLHFQ mean score at end of follow-up)	8		Mean Difference (Random, 95% CI)	Totals not selected
14 Quality of life (subgroup by length of intervention)	8		Mean Difference (Random, 95% CI)	-5.76 [-10.64, -0.88]
14.1 Less than 6 months' follow-up	6		Mean Difference (Random, 95% CI)	-3.32 [-8.59, 1.96]
14.2 More than 6 months' follow-up	2		Mean Difference (Random, 95% CI)	-12.14 [-16.48, -7.79]
15 Quality of life (subgroup by person delivering intervention)	8		Mean Difference (Random, 95% CI)	-5.76 [-10.64, -0.88]
15.1 Specialist nurse	6		Mean Difference (Random, 95% CI)	-7.87 [-14.36, -1.39]
15.2 Nurse/community nurse	2		Mean Difference (Random, 95% CI)	-0.91 [-8.48, 6.67]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.3 Pharmacist/community pharmacist	0		Mean Difference (Random, 95% CI)	0.0 [0.0, 0.0]
15.4 Multidisciplinary	0		Mean Difference (Random, 95% CI)	0.0 [0.0, 0.0]
15.5 Other	0		Mean Difference (Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 Case management vs usual care, Outcome 1 All-cause mortality - main analysis.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Aldamiz-Echevarria 2007	22/137	21/142		4.56%	1.09[0.63,1.88]
Atienza 2004	30/164	51/174		6.82%	0.62[0.42,0.93]
Berger 2010	21/96	35/90		5.79%	0.56[0.36,0.89]
Blue 2001	25/84	25/81		5.72%	0.96[0.61,1.53]
Brotons 2009	26/144	29/138		5.54%	0.86[0.53,1.38]
de Souza 2014	10/123	18/129		2.97%	0.58[0.28,1.21]
DeBusk 2004	21/228	29/234		4.78%	0.74[0.44,1.26]
Dunbar 2014	2/70	2/64		0.52%	0.91[0.13,6.3]
Holland 2007	30/169	24/170		5.28%	1.26[0.77,2.06]
Jaarsma 2000	22/84	16/95		4.3%	1.56[0.88,2.76]
Jaarsma 2008	83/344	99/339		10.13%	0.83[0.64,1.06]
Kasper 2002	7/102	13/98		2.21%	0.52[0.22,1.24]
Kimmelstiel 2004	11/103	14/97		2.92%	0.74[0.35,1.55]
Krumholz 2002	9/44	13/44		2.92%	0.69[0.33,1.45]
Kwok 2008	4/49	8/56		1.39%	0.57[0.18,1.78]
Leventhal 2011	2/22	4/20		0.75%	0.45[0.09,2.22]
Lopez 2006	9/70	19/64		3.07%	0.43[0.21,0.89]
Mehralian 2014	2/55	4/55		0.69%	0.5[0.1,2.62]
Naylor 2004	11/118	32/121		3.69%	0.35[0.19,0.67]
Nucifora 2006	14/99	8/101		2.45%	1.79[0.78,4.07]
Ong 2016	100/715	114/722		10.19%	0.89[0.69,1.13]
Rainville 1999	1/17	4/17		0.44%	0.25[0.03,2.01]
Stewart 1999a	18/100	28/100		4.88%	0.64[0.38,1.08]
Tsuchihashi-Makaya 2013	8/79	8/82		1.99%	1.04[0.41,2.63]
Tsuyuki 2004	16/140	12/136		3.12%	1.3[0.64,2.64]
Yu 2015a	9/90	17/88		2.84%	0.52[0.24,1.1]
Total (95% CI)	**3446**	**3457**		**100%**	**0.78[0.68,0.9]**
Total events: 513 (Case management), 647 (Usual care)					
Heterogeneity: Tau^2=0.03; Chi^2=35.94, df=25(P=0.07); I^2=30.44%					
Test for overall effect: Z=3.39(P=0)					

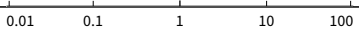


Favours case management

Favours usual care

Analysis 1.2. Comparison 1 Case management vs usual care, Outcome 2 All-cause mortality - subgroup analysis by length of follow-up.

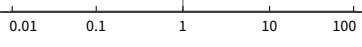
Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 6 months' follow-up					
de Souza 2014	10/123	18/129		2.97%	0.58[0.28,1.21]
Dunbar 2014	2/70	2/64		0.52%	0.91[0.13,6.3]
Holland 2007	30/169	24/170		5.28%	1.26[0.77,2.06]
Kasper 2002	7/102	13/98		2.21%	0.52[0.22,1.24]
Kwok 2008	4/49	8/56		1.39%	0.57[0.18,1.78]
Mehralian 2014	2/55	4/55		0.69%	0.5[0.1,2.62]
Nucifora 2006	14/99	8/101		2.45%	1.79[0.78,4.07]
Ong 2016	100/715	114/722		10.19%	0.89[0.69,1.13]
Stewart 1999a	18/100	28/100		4.88%	0.64[0.38,1.08]
Tsuyuki 2004	16/140	12/136		3.12%	1.3[0.64,2.64]
Subtotal (95% CI)	**1622**	**1631**		**33.71%**	**0.88[0.7,1.11]**
Total events: 203 (Case management), 231 (Usual care)					
Heterogeneity: Tau^2=0.02; Chi^2=11, df=9(P=0.28); I^2=18.19%					
Test for overall effect: Z=1.09(P=0.28)					
1.2.2 More than 6 months' follow-up					
Aldamiz-Echevarria 2007	22/137	21/142		4.56%	1.09[0.63,1.88]
Atienza 2004	30/164	51/174		6.82%	0.62[0.42,0.93]
Berger 2010	21/96	35/90		5.79%	0.56[0.36,0.89]
Blue 2001	25/84	25/81		5.72%	0.96[0.61,1.53]
Brotons 2009	26/144	29/138		5.54%	0.86[0.53,1.38]
DeBusk 2004	21/228	29/234		4.78%	0.74[0.44,1.26]
Jaarsma 2000	22/84	16/95		4.3%	1.56[0.88,2.76]
Jaarsma 2008	83/344	99/339		10.13%	0.83[0.64,1.06]
Kimmelstiel 2004	11/103	14/97		2.92%	0.74[0.35,1.55]
Krumholz 2002	9/44	13/44		2.92%	0.69[0.33,1.45]
Leventhal 2011	2/22	4/20		0.75%	0.45[0.09,2.22]
Lopez 2006	9/70	19/64		3.07%	0.43[0.21,0.89]
Naylor 2004	11/118	32/121		3.69%	0.35[0.19,0.67]
Rainville 1999	1/17	4/17		0.44%	0.25[0.03,2.01]
Tsuchihashi-Makaya 2013	8/79	8/82		1.99%	1.04[0.41,2.63]
Yu 2015a	9/90	17/88		2.84%	0.52[0.24,1.1]
Subtotal (95% CI)	**1824**	**1826**		**66.29%**	**0.74[0.62,0.88]**
Total events: 310 (Case management), 416 (Usual care)					
Heterogeneity: Tau^2=0.04; Chi^2=22.91, df=15(P=0.09); I^2=34.53%					
Test for overall effect: Z=3.34(P=0)					
Total (95% CI)	**3446**	**3457**		**100%**	**0.78[0.68,0.9]**
Total events: 513 (Case management), 647 (Usual care)					
Heterogeneity: Tau^2=0.03; Chi^2=35.94, df=25(P=0.07); I^2=30.44%					
Test for overall effect: Z=3.39(P=0)					
Test for subgroup differences: Chi^2=1.48, df=1 (P=0.22), I^2=32.51%					



Favours case management — Favours usual care

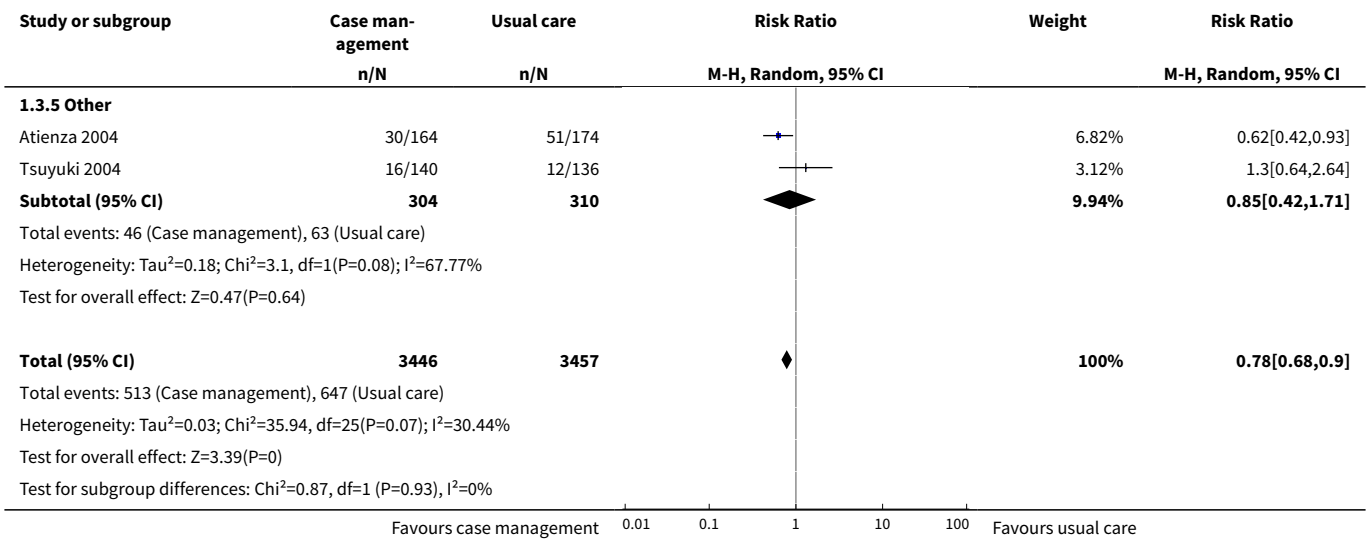
Analysis 1.3. Comparison 1 Case management vs usual care, Outcome 3 All-cause mortality - subgroup analysis by person delivering the intervention.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.3.1 Specialist nurse					
Blue 2001	25/84	25/81		5.72%	0.96[0.61,1.53]
Brotons 2009	26/144	29/138		5.54%	0.86[0.53,1.38]
Dunbar 2014	2/70	2/64		0.52%	0.91[0.13,6.3]
Jaarsma 2000	22/84	16/95		4.3%	1.56[0.88,2.76]
Kasper 2002	7/102	13/98		2.21%	0.52[0.22,1.24]
Kimmelstiel 2004	11/103	14/97		2.92%	0.74[0.35,1.55]
Krumholz 2002	9/44	13/44		2.92%	0.69[0.33,1.45]
Leventhal 2011	2/22	4/20		0.75%	0.45[0.09,2.22]
Naylor 2004	11/118	32/121		3.69%	0.35[0.19,0.67]
Nucifora 2006	14/99	8/101		2.45%	1.79[0.78,4.07]
Stewart 1999a	18/100	28/100		4.88%	0.64[0.38,1.08]
Tsuchihashi-Makaya 2013	8/79	8/82		1.99%	1.04[0.41,2.63]
Yu 2015a	9/90	17/88		2.84%	0.52[0.24,1.1]
Subtotal (95% CI)	**1139**	**1129**		**40.74%**	**0.79[0.61,1.01]**
Total events: 164 (Case management), 209 (Usual care)					
Heterogeneity: Tau^2=0.08; Chi^2=19.85, df=12(P=0.07); I^2=39.55%					
Test for overall effect: Z=1.85(P=0.06)					
1.3.2 Nurse/community nurse					
Aldamiz-Echevarria 2007	22/137	21/142		4.56%	1.09[0.63,1.88]
de Souza 2014	10/123	18/129		2.97%	0.58[0.28,1.21]
DeBusk 2004	21/228	29/234		4.78%	0.74[0.44,1.26]
Kwok 2008	4/49	8/56		1.39%	0.57[0.18,1.78]
Mehralian 2014	2/55	4/55		0.69%	0.5[0.1,2.62]
Ong 2016	100/715	114/722		10.19%	0.89[0.69,1.13]
Subtotal (95% CI)	**1307**	**1338**		**24.6%**	**0.84[0.69,1.03]**
Total events: 159 (Case management), 194 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=3, df=5(P=0.7); I^2=0%					
Test for overall effect: Z=1.7(P=0.09)					
1.3.3 Pharmacist/community pharmacist					
Holland 2007	30/169	24/170		5.28%	1.26[0.77,2.06]
Lopez 2006	9/70	19/64		3.07%	0.43[0.21,0.89]
Rainville 1999	1/17	4/17		0.44%	0.25[0.03,2.01]
Subtotal (95% CI)	**256**	**251**		**8.8%**	**0.65[0.25,1.67]**
Total events: 40 (Case management), 47 (Usual care)					
Heterogeneity: Tau^2=0.45; Chi^2=7.16, df=2(P=0.03); I^2=72.08%					
Test for overall effect: Z=0.9(P=0.37)					
1.3.4 Multidisciplinary					
Berger 2010	21/96	35/90		5.79%	0.56[0.36,0.89]
Jaarsma 2008	83/344	99/339		10.13%	0.83[0.64,1.06]
Subtotal (95% CI)	**440**	**429**		**15.92%**	**0.72[0.5,1.03]**
Total events: 104 (Case management), 134 (Usual care)					
Heterogeneity: Tau^2=0.04; Chi^2=2.08, df=1(P=0.15); I^2=51.99%					
Test for overall effect: Z=1.8(P=0.07)					

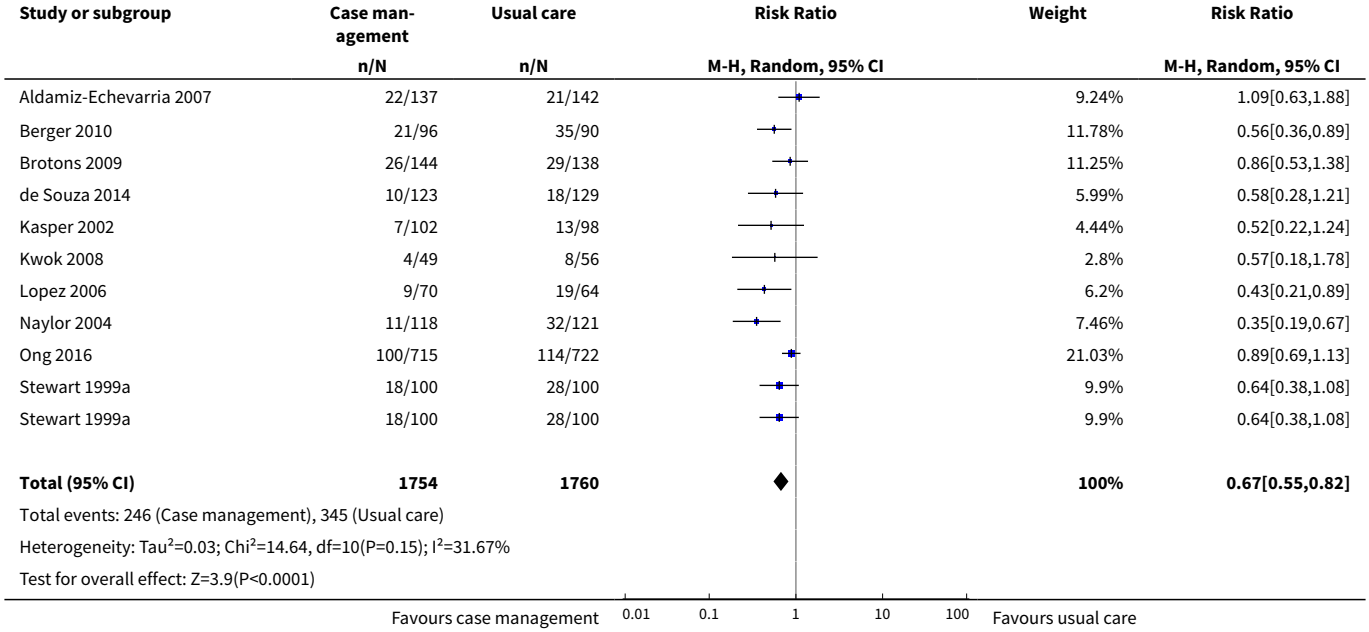


Favours case management

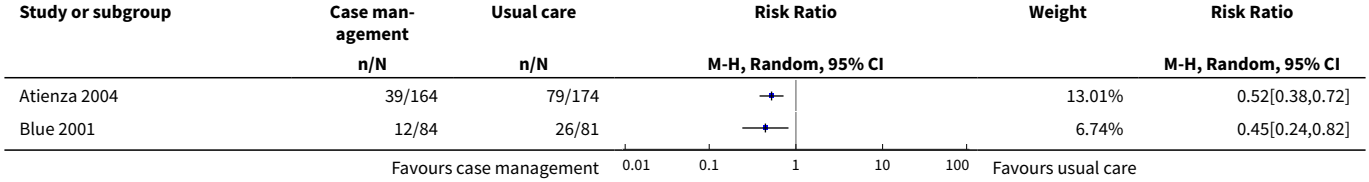
Favours usual care

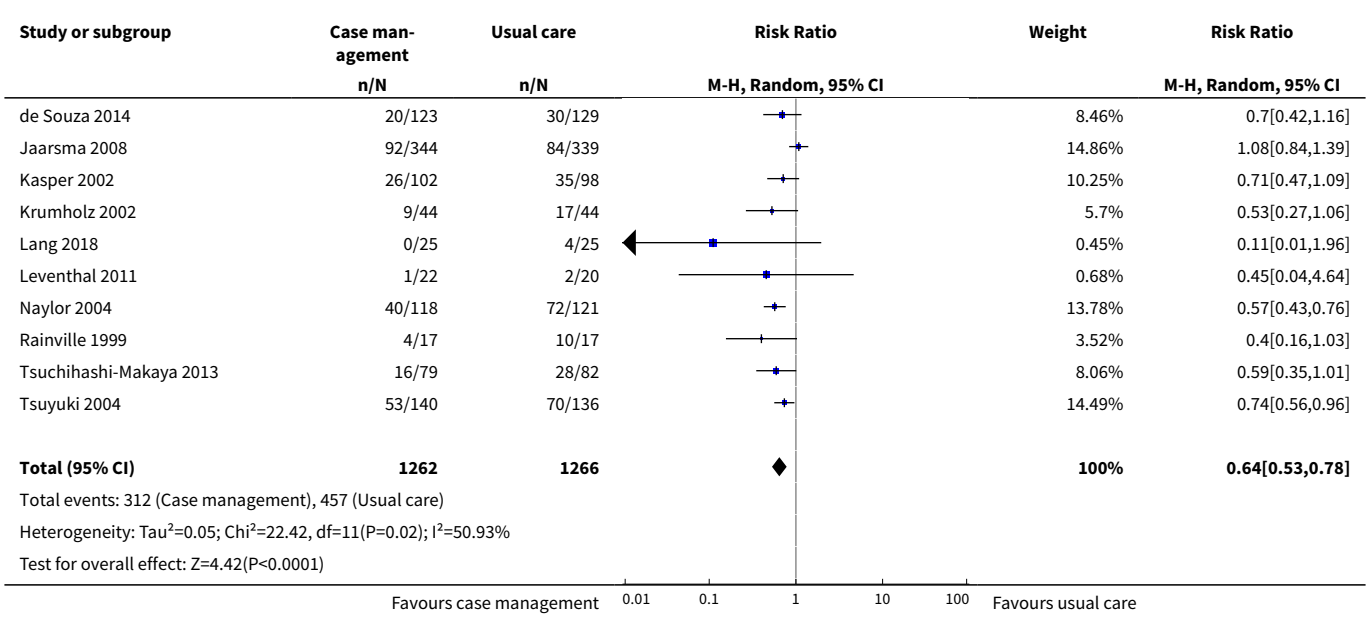


Analysis 1.4. Comparison 1 Case management vs usual care, Outcome 4 All-cause mortality - sensitivity analysis with low risk of bias.

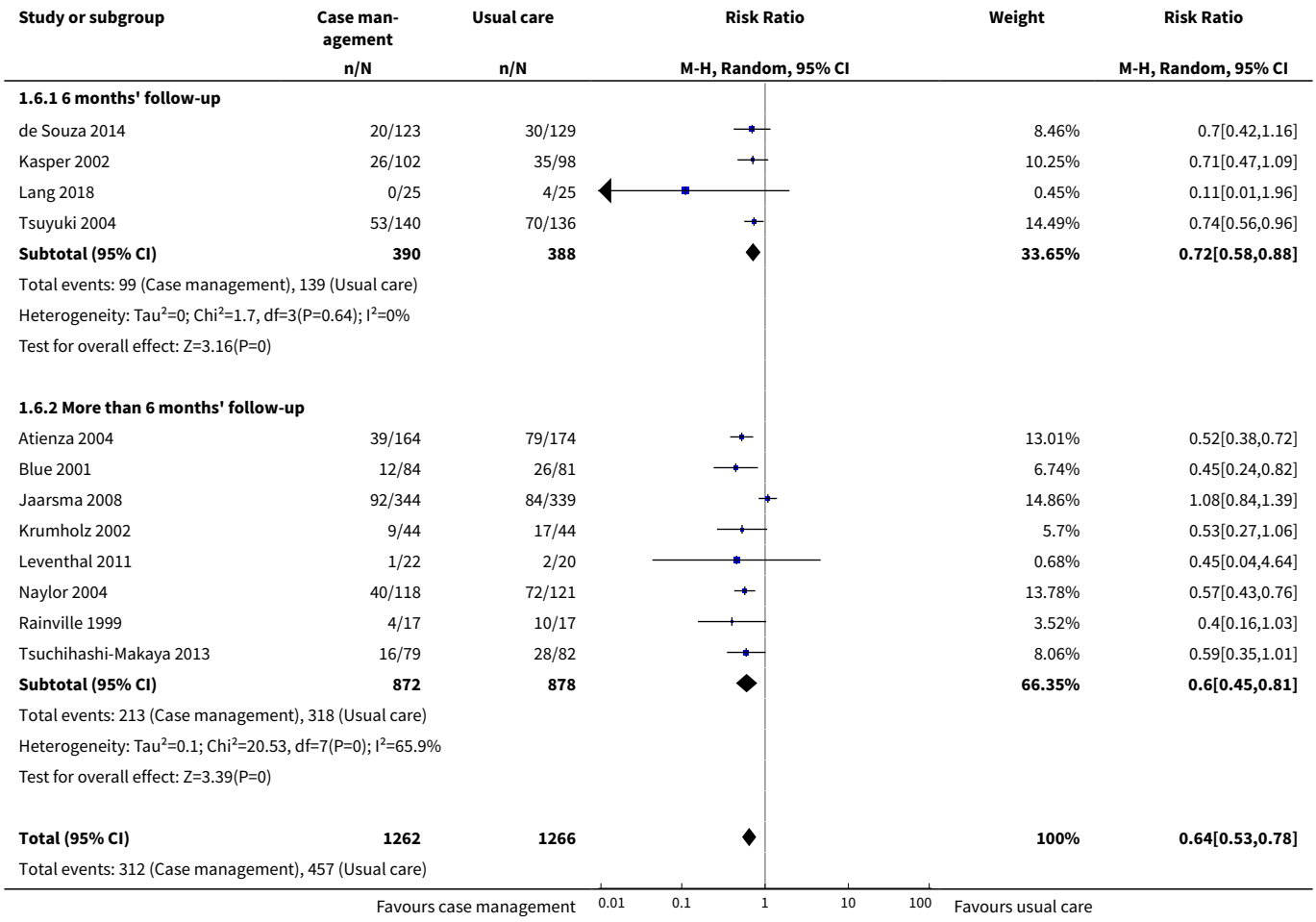


Analysis 1.5. Comparison 1 Case management vs usual care, Outcome 5 HF readmissions - main analysis.





Analysis 1.6. Comparison 1 Case management vs usual care, Outcome 6 HF readmissions - subgroup analysis by length of follow-up.



Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Heterogeneity: Tau²=0.05; Chi²=22.42, df=11(P=0.02); I²=50.93%					
Test for overall effect: Z=4.42(P<0.0001)					
Test for subgroup differences: Chi²=0.94, df=1 (P=0.33), I²=0%					

Favours case management 0.01 0.1 1 10 100 Favours usual care

Analysis 1.7. Comparison 1 Case management vs usual care, Outcome 7 HF readmissions - subgroup analysis by person delivering the intervention.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Specialist nurse					
Blue 2001	12/84	26/81		6.74%	0.45[0.24,0.82]
Kasper 2002	26/102	35/98		10.25%	0.71[0.47,1.09]
Krumholz 2002	9/44	17/44		5.7%	0.53[0.27,1.06]
Lang 2018	0/25	4/25		0.45%	0.11[0.01,1.96]
Leventhal 2011	1/22	2/20		0.68%	0.45[0.04,4.64]
Naylor 2004	40/118	72/121		13.78%	0.57[0.43,0.76]
Tsuchihashi-Makaya 2013	16/79	28/82		8.06%	0.59[0.35,1.01]
Subtotal (95% CI)	**474**	**471**		**45.66%**	**0.58[0.47,0.7]**
Total events: 104 (Case management), 184 (Usual care)					
Heterogeneity: Tau²=0; Chi²=3.07, df=6(P=0.8); I²=0%					
Test for overall effect: Z=5.48(P<0.0001)					
1.7.2 Nurse/community nurse					
de Souza 2014	20/123	30/129		8.46%	0.7[0.42,1.16]
Subtotal (95% CI)	**123**	**129**		**8.46%**	**0.7[0.42,1.16]**
Total events: 20 (Case management), 30 (Usual care)					
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%					
Test for overall effect: Z=1.38(P=0.17)					
1.7.3 Pharmacist/community pharmacist					
Rainville 1999	4/17	10/17		3.52%	0.4[0.16,1.03]
Subtotal (95% CI)	**17**	**17**		**3.52%**	**0.4[0.16,1.03]**
Total events: 4 (Case management), 10 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.9(P=0.06)					
1.7.4 Multidisciplinary					
Jaarsma 2008	92/344	84/339		14.86%	1.08[0.84,1.39]
Subtotal (95% CI)	**344**	**339**		**14.86%**	**1.08[0.84,1.39]**
Total events: 92 (Case management), 84 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.59(P=0.56)					
1.7.5 Other					
Atienza 2004	39/164	79/174		13.01%	0.52[0.38,0.72]
Tsuyuki 2004	53/140	70/136		14.49%	0.74[0.56,0.96]
Subtotal (95% CI)	**304**	**310**		**27.49%**	**0.63[0.45,0.88]**

Favours case management 0.01 0.1 1 10 100 Favours usual care

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 92 (Case management), 149 (Usual care)					
Heterogeneity: Tau²=0.04; Chi²=2.6, df=1(P=0.11); I²=61.5%					
Test for overall effect: Z=2.73(P=0.01)					
Total (95% CI)	**1262**	**1266**		**100%**	**0.64[0.53,0.78]**
Total events: 312 (Case management), 457 (Usual care)					
Heterogeneity: Tau²=0.05; Chi²=22.42, df=11(P=0.02); I²=50.93%					
Test for overall effect: Z=4.42(P<0.0001)					
Test for subgroup differences: Chi²=16.54, df=1 (P=0), I²=75.82%					

Favours case management 0.01 0.1 1 10 100 Favours usual care

Analysis 1.8. Comparison 1 Case management vs usual care, Outcome 8 HF readmissions - sensitivity analysis with low risk of bias.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
de Souza 2014	20/123	30/129		18.15%	0.7[0.42,1.16]
Kasper 2002	26/102	35/98		26.03%	0.71[0.47,1.09]
Lang 2018	0/25	4/25		0.57%	0.11[0.01,1.96]
Naylor 2004	40/118	72/121		55.26%	0.57[0.43,0.76]
Total (95% CI)	**368**	**373**		**100%**	**0.62[0.5,0.77]**
Total events: 86 (Case management), 141 (Usual care)					
Heterogeneity: Tau²=0; Chi²=2.34, df=3(P=0.51); I²=0%					
Test for overall effect: Z=4.3(P<0.0001)					

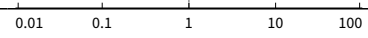
Favours case management 0.01 0.1 1 10 100 Favours usual care

Analysis 1.9. Comparison 1 Case management vs usual care, Outcome 9 All-cause readmissions - main analysis.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Atienza 2004	68/164	101/174		9.56%	0.71[0.57,0.89]
Blue 2001	47/84	49/81		8%	0.92[0.71,1.2]
de Souza 2014	38/123	49/129		5.45%	0.81[0.58,1.15]
DeBusk 2004	116/227	117/234		11.64%	1.02[0.85,1.22]
Jaarsma 2000	31/85	47/94		5.41%	0.73[0.52,1.03]
Jaarsma 2008	194/344	181/339		14.3%	1.06[0.92,1.21]
Kwok 2008	23/49	32/56		4.81%	0.82[0.56,1.19]
Lang 2018	4/25	7/25		0.71%	0.57[0.19,1.71]
Leventhal 2011	10/22	6/20		1.26%	1.52[0.67,3.41]
Lopez 2006	23/70	31/64		4.02%	0.68[0.45,1.03]
Naylor 2004	53/118	67/121		8.11%	0.81[0.63,1.05]
Ong 2016	363/715	355/722		16.38%	1.03[0.93,1.15]
Tsuyuki 2004	59/140	51/136		6.89%	1.12[0.84,1.5]

Favours case management 0.01 0.1 1 10 100 Favours usual care

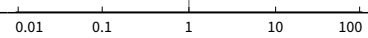
Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Yu 2015a	25/90	27/88		3.48%	0.91[0.57,1.43]
Total (95% CI)	**2256**	**2283**		**100%**	**0.92[0.83,1.01]**
Total events: 1054 (Case management), 1120 (Usual care)					
Heterogeneity: Tau^2=0.01; Chi^2=22.78, df=13(P=0.04); I^2=42.92%					
Test for overall effect: Z=1.82(P=0.07)					



Favours case management — Favours usual care

Analysis 1.10. Comparison 1 Case management vs usual care, Outcome 10 All-cause readmissions - subgroup analysis by length of follow-up.

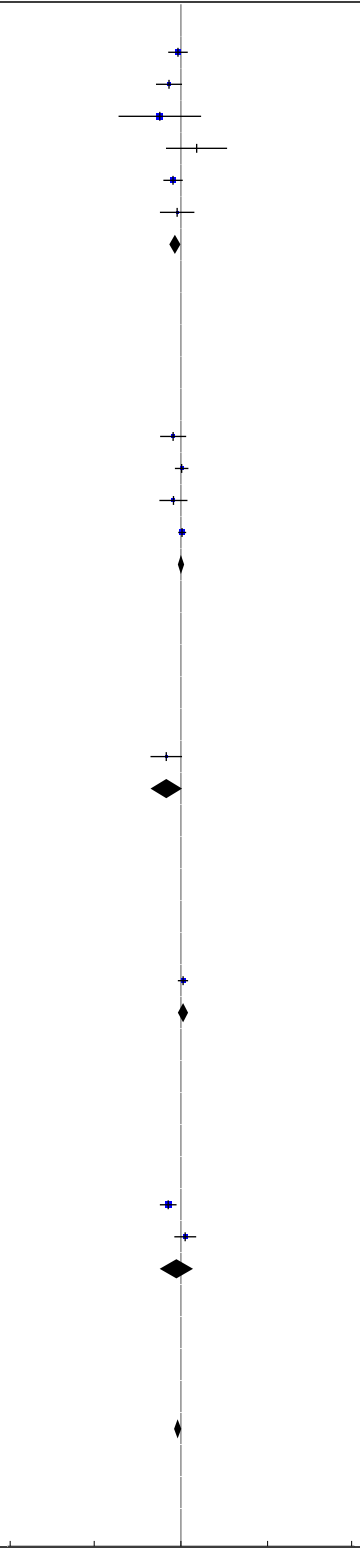
Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 6 months' follow-up					
de Souza 2014	38/123	49/129		5.45%	0.81[0.58,1.15]
Kwok 2008	23/49	32/56		4.81%	0.82[0.56,1.19]
Lang 2018	4/25	7/25		0.71%	0.57[0.19,1.71]
Ong 2016	363/715	355/722		16.38%	1.03[0.93,1.15]
Tsuyuki 2004	59/140	51/136		6.89%	1.12[0.84,1.5]
Subtotal (95% CI)	**1052**	**1068**		**34.23%**	**0.99[0.89,1.11]**
Total events: 487 (Case management), 494 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=4.42, df=4(P=0.35); I^2=9.6%					
Test for overall effect: Z=0.12(P=0.91)					
1.10.2 More than 6 months' follow-up					
Atienza 2004	68/164	101/174		9.56%	0.71[0.57,0.89]
Blue 2001	47/84	49/81		8%	0.92[0.71,1.2]
DeBusk 2004	116/227	117/234		11.64%	1.02[0.85,1.22]
Jaarsma 2000	31/85	47/94		5.41%	0.73[0.52,1.03]
Jaarsma 2008	194/344	181/339		14.3%	1.06[0.92,1.21]
Leventhal 2011	10/22	6/20		1.26%	1.52[0.67,3.41]
Lopez 2006	23/70	31/64		4.02%	0.68[0.45,1.03]
Naylor 2004	53/118	67/121		8.11%	0.81[0.63,1.05]
Yu 2015a	25/90	27/88		3.48%	0.91[0.57,1.43]
Subtotal (95% CI)	**1204**	**1215**		**65.77%**	**0.89[0.78,1.01]**
Total events: 567 (Case management), 626 (Usual care)					
Heterogeneity: Tau^2=0.02; Chi^2=16.48, df=8(P=0.04); I^2=51.45%					
Test for overall effect: Z=1.84(P=0.07)					
Total (95% CI)	**2256**	**2283**		**100%**	**0.92[0.83,1.01]**
Total events: 1054 (Case management), 1120 (Usual care)					
Heterogeneity: Tau^2=0.01; Chi^2=22.78, df=13(P=0.04); I^2=42.92%					
Test for overall effect: Z=1.82(P=0.07)					
Test for subgroup differences: Chi^2=1.7, df=1 (P=0.19), I^2=41.27%					



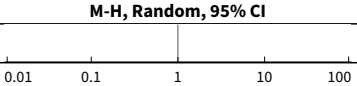
Favours case management — Favours usual care

Analysis 1.11. Comparison 1 Case management vs usual care, Outcome 11 All-cause readmissions - subgroup analysis by person delivering the intervention.

Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.11.1 Specialist nurse					
Blue 2001	47/84	49/81		8%	0.92[0.71,1.2]
Jaarsma 2000	31/85	47/94		5.41%	0.73[0.52,1.03]
Lang 2018	4/25	7/25		0.71%	0.57[0.19,1.71]
Leventhal 2011	10/22	6/20		1.26%	1.52[0.67,3.41]
Naylor 2004	53/118	67/121		8.11%	0.81[0.63,1.05]
Yu 2015a	25/90	27/88		3.48%	0.91[0.57,1.43]
Subtotal (95% CI)	**424**	**429**		**26.97%**	**0.85[0.73,0.99]**
Total events: 170 (Case management), 203 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=3.82, df=5(P=0.58); I^2=0%					
Test for overall effect: Z=2.12(P=0.03)					
1.11.2 Nurse/community nurse					
de Souza 2014	38/123	49/129		5.45%	0.81[0.58,1.15]
DeBusk 2004	116/227	117/234		11.64%	1.02[0.85,1.22]
Kwok 2008	23/49	32/56		4.81%	0.82[0.56,1.19]
Ong 2016	363/715	355/722		16.38%	1.03[0.93,1.15]
Subtotal (95% CI)	**1114**	**1141**		**38.27%**	**1[0.92,1.09]**
Total events: 540 (Case management), 553 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=2.87, df=3(P=0.41); I^2=0%					
Test for overall effect: Z=0.08(P=0.93)					
1.11.3 Pharmacist/community pharmacist					
Lopez 2006	23/70	31/64		4.02%	0.68[0.45,1.03]
Subtotal (95% CI)	**70**	**64**		**4.02%**	**0.68[0.45,1.03]**
Total events: 23 (Case management), 31 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.81(P=0.07)					
1.11.4 Multidisciplinary					
Jaarsma 2008	194/344	181/339		14.3%	1.06[0.92,1.21]
Subtotal (95% CI)	**344**	**339**		**14.3%**	**1.06[0.92,1.21]**
Total events: 194 (Case management), 181 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.79(P=0.43)					
1.11.5 Other					
Atienza 2004	68/164	101/174		9.56%	0.71[0.57,0.89]
Tsuyuki 2004	59/140	51/136		6.89%	1.12[0.84,1.5]
Subtotal (95% CI)	**304**	**310**		**16.45%**	**0.89[0.57,1.38]**
Total events: 127 (Case management), 152 (Usual care)					
Heterogeneity: Tau^2=0.09; Chi^2=5.92, df=1(P=0.01); I^2=83.12%					
Test for overall effect: Z=0.53(P=0.6)					
Total (95% CI)	**2256**	**2283**		**100%**	**0.92[0.83,1.01]**
Total events: 1054 (Case management), 1120 (Usual care)					
Heterogeneity: Tau^2=0.01; Chi^2=22.78, df=13(P=0.04); I^2=42.92%					
Test for overall effect: Z=1.82(P=0.07)					



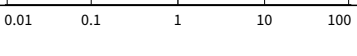
Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Test for subgroup differences: Chi²=8, df=1 (P=0.09), I²=50.02%					



Favours case management | Favours usual care

Analysis 1.12. Comparison 1 Case management vs usual care, Outcome 12 All-cause readmissions - sensitivity analysis with low risk of bias.

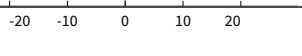
Study or subgroup	Case management n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
de Souza 2014	38/123	49/129		14.83%	0.81[0.58,1.15]
Kwok 2008	23/49	32/56		13.23%	0.82[0.56,1.19]
Lang 2018	4/25	7/25		2.09%	0.57[0.19,1.71]
Lopez 2006	23/70	31/64		11.21%	0.68[0.45,1.03]
Naylor 2004	53/118	67/121		21.1%	0.81[0.63,1.05]
Ong 2016	363/715	355/722		37.54%	1.03[0.93,1.15]
Total (95% CI)	**1100**	**1117**		**100%**	**0.87[0.74,1.02]**
Total events: 504 (Case management), 541 (Usual care)					
Heterogeneity: Tau²=0.02; Chi²=8.64, df=5(P=0.12); I²=42.15%					
Test for overall effect: Z=1.74(P=0.08)					



Favours case management | Favours usual care

Analysis 1.13. Comparison 1 Case management vs usual care, Outcome 13 Quality of life (MLHFQ mean score at end of follow-up).

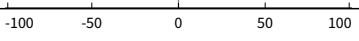
Study or subgroup	case management N	usual care N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Brotons 2009	101	97	-12.5 (2.755)		-12.54[-17.94,-7.14]
Dunbar 2014	54	54	-6.3 (4.937)		-6.3[-15.98,3.38]
Holland 2007	78	80	3.7 (3.776)		3.73[-3.67,11.13]
Kasper 2002	94	85	-12.6 (3.766)		-12.6[-19.98,-5.22]
Lang 2018	22	23	-9.5 (8.346)		-9.5[-25.86,6.86]
Nucifora 2006	74	75	4 (2.97)		4[-1.82,9.82]
Ong 2016	383	413	-4.1 (1.774)		-4.13[-7.61,-0.65]
Yu 2015a	70	50	-11.4 (3.732)		-11.4[-18.71,-4.09]



Favours case management | Favours usual care

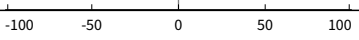
Analysis 1.14. Comparison 1 Case management vs usual care, Outcome 14 Quality of life (subgroup by length of intervention).

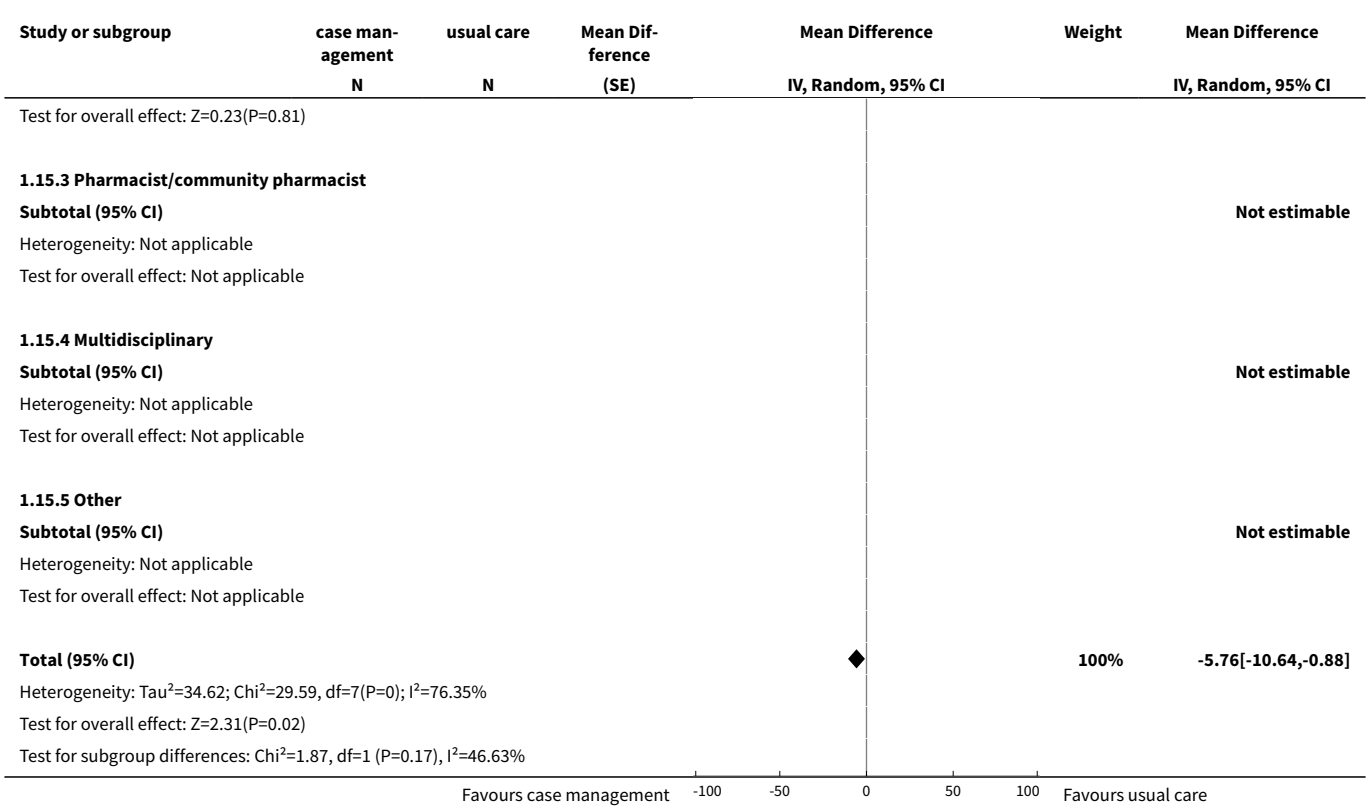
Study or subgroup	case management N	usual care N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.14.1 Less than 6 months' follow-up						
Dunbar 2014	54	54	-6.3 (4.937)		10.51%	-6.3[-15.98,3.38]
Holland 2007	0	0	3.7 (3.776)		12.69%	3.73[-3.67,11.13]
Kasper 2002	94	85	-12.6 (3.766)		12.7%	-12.6[-19.98,-5.22]
Lang 2018	22	23	-9.5 (8.346)		5.95%	-9.5[-25.86,6.86]
Nucifora 2006	74	75	4 (2.97)		14.27%	4[-1.82,9.82]
Ong 2016	383	413	-4.1 (1.774)		16.42%	-4.13[-7.61,-0.65]
Subtotal (95% CI)					**72.54%**	**-3.32[-8.59,1.96]**
Heterogeneity: Tau²=27.38; Chi²=16.69, df=5(P=0.01); I²=70.04%						
Test for overall effect: Z=1.23(P=0.22)						
1.14.2 More than 6 months' follow-up						
Brotons 2009	101	97	-12.5 (2.755)		14.69%	-12.54[-17.94,-7.14]
Yu 2015a	70	50	-11.4 (3.732)		12.77%	-11.4[-18.71,-4.09]
Subtotal (95% CI)					**27.46%**	**-12.14[-16.48,-7.79]**
Heterogeneity: Tau²=0; Chi²=0.06, df=1(P=0.81); I²=0%						
Test for overall effect: Z=5.48(P<0.0001)						
Total (95% CI)					**100%**	**-5.76[-10.64,-0.88]**
Heterogeneity: Tau²=34.62; Chi²=29.59, df=7(P=0); I²=76.35%						
Test for overall effect: Z=2.31(P=0.02)						
Test for subgroup differences: Chi²=6.4, df=1 (P=0.01), I²=84.38%						



Analysis 1.15. Comparison 1 Case management vs usual care, Outcome 15 Quality of life (subgroup by person delivering intervention).

Study or subgroup	case management N	usual care N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1.15.1 Specialist nurse						
Brotons 2009	101	97	-12.5 (2.755)		14.69%	-12.54[-17.94,-7.14]
Dunbar 2014	54	54	-6.3 (4.937)		10.51%	-6.3[-15.98,3.38]
Kasper 2002	94	85	-12.6 (3.766)		12.7%	-12.6[-19.98,-5.22]
Lang 2018	22	23	-9.5 (8.346)		5.95%	-9.5[-25.86,6.86]
Nucifora 2006	74	75	4 (2.97)		14.27%	4[-1.82,9.82]
Yu 2015a	70	50	-11.4 (3.732)		12.77%	-11.4[-18.71,-4.09]
Subtotal (95% CI)					**70.9%**	**-7.87[-14.36,-1.39]**
Heterogeneity: Tau²=47.15; Chi²=21.39, df=5(P=0); I²=76.62%						
Test for overall effect: Z=2.38(P=0.02)						
1.15.2 Nurse/community nurse						
Holland 2007	0	0	3.7 (3.776)		12.69%	3.73[-3.67,11.13]
Ong 2016	383	413	-4.1 (1.774)		16.42%	-4.13[-7.61,-0.65]
Subtotal (95% CI)					**29.1%**	**-0.91[-8.48,6.67]**
Heterogeneity: Tau²=22.19; Chi²=3.55, df=1(P=0.06); I²=71.83%						





Comparison 2. Clinic-based intervention vs usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All-cause mortality - main analysis	7	1686	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.68, 1.10]
2 All-cause mortality - subgroup analysis by length of follow-up	7	1686	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.68, 1.10]
2.1 6 months' follow-up	2	306	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.32, 1.27]
2.2 More than 6 months' follow-up	5	1380	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.67, 1.17]
3 All-cause mortality - subgroup analysis by person delivering the intervention	7	1686	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.68, 1.10]
3.1 Specialist nurse	4	1081	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.53, 1.15]
3.2 Nurse/community nurse	1	208	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.83, 1.73]
3.3 Pharmacist/community pharmacist	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
3.4 Multidisciplinary	2	397	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.47, 1.17]

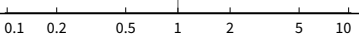
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 All-cause mortality - sensitivity analysis with low risk of bias	2	296	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.23, 1.88]
5 All-cause mortality - sensitivity analysis without cluster-RCT	6	1489	Risk Ratio (M-H, Random, 95% CI)	0.87 [0.66, 1.15]
6 HF readmissions - main analysis	2	887	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.87, 1.18]
7 HF readmissions - subgroup analysis by person delivering the intervention	2	887	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.87, 1.18]
7.1 Specialist nurse	1	679	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.77, 1.30]
7.2 Nurse/community nurse	1	208	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.84, 1.24]
7.3 Pharmacist/community pharmacist	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
7.4 Multidisciplinary	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8 HF readmissions - subgroup analysis by length of follow-up	2	887	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.87, 1.18]
8.1 6 months' follow-up	0	0	Risk Ratio (M-H, Random, 95% CI)	0.0 [0.0, 0.0]
8.2 More than 6 months' follow-up	2	887	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.87, 1.18]
9 All-cause readmissions	4	1129	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.72, 1.12]
10 All-cause readmissions - subgroup analysis by length of follow-up	4	1129	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.72, 1.12]
10.1 6 months' follow-up	1	106	Risk Ratio (M-H, Random, 95% CI)	0.51 [0.29, 0.91]
10.2 More than 6 months' follow-up	3	1023	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.85, 1.16]
11 All-cause readmissions - subgroup analysis by person delivering the intervention	4	1129	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.72, 1.12]
11.1 Specialist nurse	3	921	Risk Ratio (M-H, Random, 95% CI)	0.79 [0.52, 1.19]
11.2 Nurse/community nurse	1	208	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.84, 1.24]

Analysis 2.1. Comparison 2 Clinic-based intervention vs usual care, Outcome 1 All-cause mortality - main analysis.

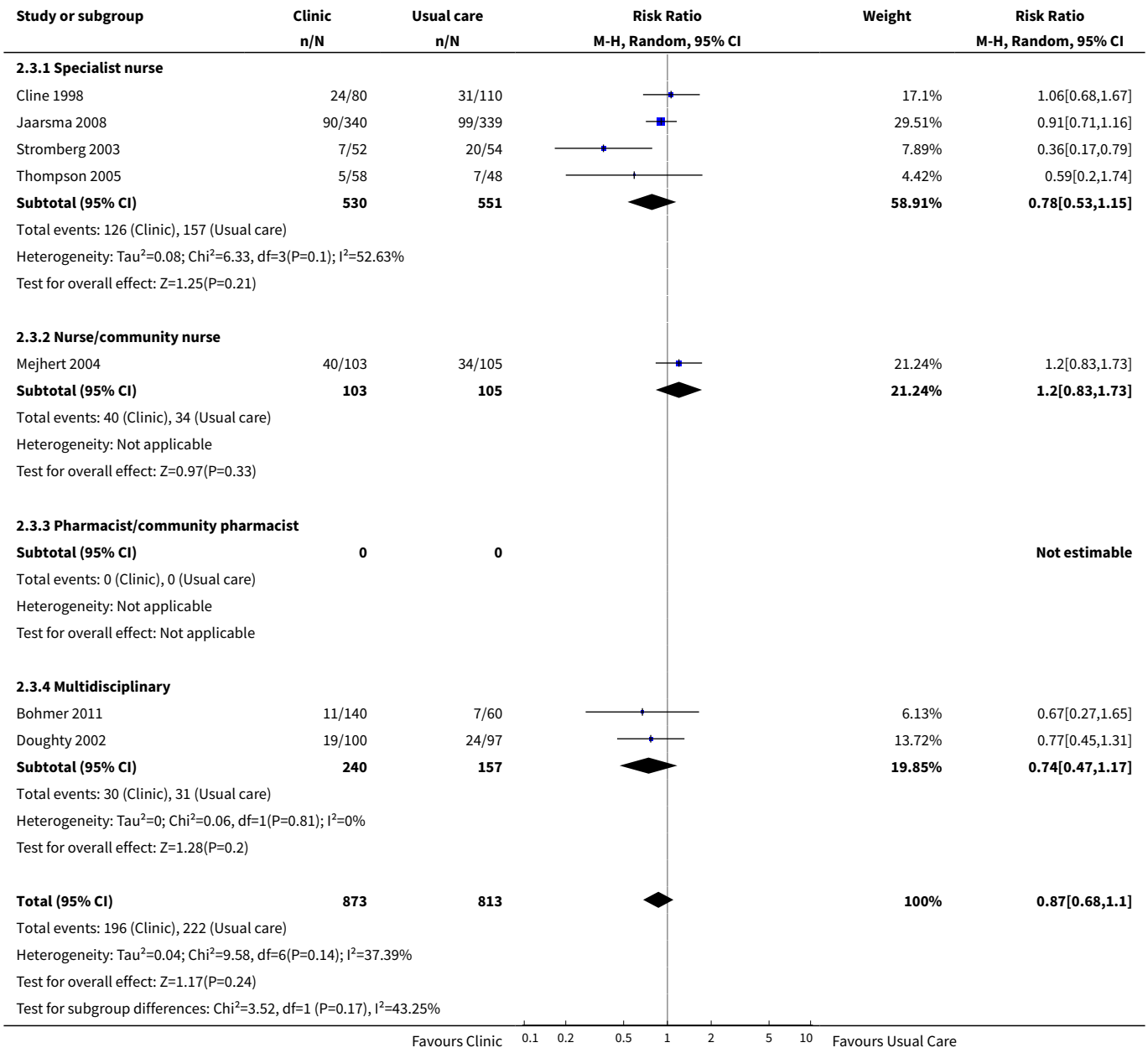
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bohmer 2011	11/140	7/60		6.13%	0.67[0.27,1.65]
Cline 1998	24/80	31/110		17.1%	1.06[0.68,1.67]
Doughty 2002	19/100	24/97		13.72%	0.77[0.45,1.31]
Jaarsma 2008	90/340	99/339		29.51%	0.91[0.71,1.16]
Mejhert 2004	40/103	34/105		21.24%	1.2[0.83,1.73]
Stromberg 2003	7/52	20/54		7.89%	0.36[0.17,0.79]
Thompson 2005	5/58	7/48		4.42%	0.59[0.2,1.74]
Total (95% CI)	**873**	**813**		**100%**	**0.87[0.68,1.1]**
Total events: 196 (Clinic), 222 (Usual care)					
Heterogeneity: Tau^2=0.04; Chi^2=9.58, df=6(P=0.14); I^2=37.39%					
Test for overall effect: Z=1.17(P=0.24)					

Analysis 2.2. Comparison 2 Clinic-based intervention vs usual care, Outcome 2 All-cause mortality - subgroup analysis by length of follow-up.

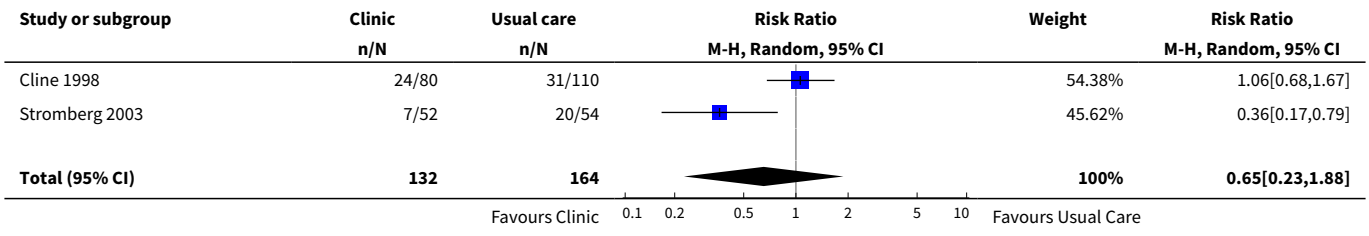
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 6 months' follow-up					
Bohmer 2011	11/140	7/60		6.13%	0.67[0.27,1.65]
Thompson 2005	5/58	7/48		4.42%	0.59[0.2,1.74]
Subtotal (95% CI)	**198**	**108**		**10.55%**	**0.64[0.32,1.27]**
Total events: 16 (Clinic), 14 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.03, df=1(P=0.86); I^2=0%					
Test for overall effect: Z=1.27(P=0.2)					
2.2.2 More than 6 months' follow-up					
Cline 1998	24/80	31/110		17.1%	1.06[0.68,1.67]
Doughty 2002	19/100	24/97		13.72%	0.77[0.45,1.31]
Jaarsma 2008	90/340	99/339		29.51%	0.91[0.71,1.16]
Mejhert 2004	40/103	34/105		21.24%	1.2[0.83,1.73]
Stromberg 2003	7/52	20/54		7.89%	0.36[0.17,0.79]
Subtotal (95% CI)	**675**	**705**		**89.45%**	**0.89[0.67,1.17]**
Total events: 180 (Clinic), 208 (Usual care)					
Heterogeneity: Tau^2=0.05; Chi^2=8.48, df=4(P=0.08); I^2=52.83%					
Test for overall effect: Z=0.83(P=0.41)					
Total (95% CI)	**873**	**813**		**100%**	**0.87[0.68,1.1]**
Total events: 196 (Clinic), 222 (Usual care)					
Heterogeneity: Tau^2=0.04; Chi^2=9.58, df=6(P=0.14); I^2=37.39%					
Test for overall effect: Z=1.17(P=0.24)					
Test for subgroup differences: Chi^2=0.76, df=1 (P=0.38), I^2=0%					



Analysis 2.3. Comparison 2 Clinic-based intervention vs usual care, Outcome 3 All-cause mortality - subgroup analysis by person delivering the intervention.



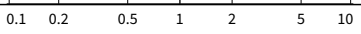
Analysis 2.4. Comparison 2 Clinic-based intervention vs usual care, Outcome 4 All-cause mortality - sensitivity analysis with low risk of bias.



Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 31 (Clinic), 51 (Usual care)					
Heterogeneity: Tau^2=0.48; Chi^2=5.66, df=1(P=0.02); I^2=82.34%					
Test for overall effect: Z=0.79(P=0.43)					

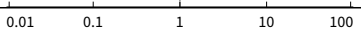
Analysis 2.5. Comparison 2 Clinic-based intervention vs usual care, Outcome 5 All-cause mortality - sensitivity analysis without cluster-RCT.

Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bohmer 2011	11/140	7/60		7.93%	0.67[0.27,1.65]
Cline 1998	24/80	31/110		20.2%	1.06[0.68,1.67]
Jaarsma 2008	90/340	99/339		31.71%	0.91[0.71,1.16]
Mejhert 2004	40/103	34/105		24.29%	1.2[0.83,1.73]
Stromberg 2003	7/52	20/54		10.06%	0.36[0.17,0.79]
Thompson 2005	5/58	7/48		5.81%	0.59[0.2,1.74]
Total (95% CI)	**773**	**716**		**100%**	**0.87[0.66,1.15]**
Total events: 177 (Clinic), 198 (Usual care)					
Heterogeneity: Tau^2=0.05; Chi^2=9.17, df=5(P=0.1); I^2=45.47%					
Test for overall effect: Z=0.96(P=0.34)					



Analysis 2.6. Comparison 2 Clinic-based intervention vs usual care, Outcome 6 HF readmissions - main analysis.

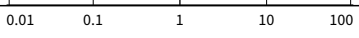
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Jaarsma 2008	84/340	84/339		35.25%	1[0.77,1.3]
Mejhert 2004	69/103	69/105		64.75%	1.02[0.84,1.24]
Total (95% CI)	**443**	**444**		**100%**	**1.01[0.87,1.18]**
Total events: 153 (Clinic), 153 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					



Analysis 2.7. Comparison 2 Clinic-based intervention vs usual care, Outcome 7 HF readmissions - subgroup analysis by person delivering the intervention.

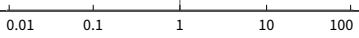
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.7.1 Specialist nurse					
Jaarsma 2008	84/340	84/339		35.25%	1[0.77,1.3]
Subtotal (95% CI)	**340**	**339**		**35.25%**	**1[0.77,1.3]**

Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total events: 84 (Clinic), 84 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.02(P=0.98)					
2.7.2 Nurse/community nurse					
Mejhert 2004	69/103	69/105		64.75%	1.02[0.84,1.24]
Subtotal (95% CI)	**103**	**105**		**64.75%**	**1.02[0.84,1.24]**
Total events: 69 (Clinic), 69 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.19(P=0.85)					
2.7.3 Pharmacist/community pharmacist					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Clinic), 0 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.7.4 Multidisciplinary					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Clinic), 0 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
Total (95% CI)	**443**	**444**		**100%**	**1.01[0.87,1.18]**
Total events: 153 (Clinic), 153 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					
Test for subgroup differences: Chi^2=0.02, df=1 (P=0.89), I^2=0%					



Analysis 2.8. Comparison 2 Clinic-based intervention vs usual care, Outcome 8 HF readmissions - subgroup analysis by length of follow-up.

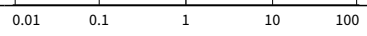
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.8.1 6 months' follow-up					
Subtotal (95% CI)	**0**	**0**			**Not estimable**
Total events: 0 (Clinic), 0 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Not applicable					
2.8.2 More than 6 months' follow-up					
Jaarsma 2008	84/340	84/339		35.25%	1[0.77,1.3]
Mejhert 2004	69/103	69/105		64.75%	1.02[0.84,1.24]
Subtotal (95% CI)	**443**	**444**		**100%**	**1.01[0.87,1.18]**
Total events: 153 (Clinic), 153 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					



Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Total (95% CI)	**443**	**444**		**100%**	**1.01[0.87,1.18]**
Total events: 153 (Clinic), 153 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.89); I^2=0%					
Test for overall effect: Z=0.14(P=0.89)					
Test for subgroup differences: Not applicable					

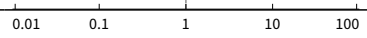
Analysis 2.9. Comparison 2 Clinic-based intervention vs usual care, Outcome 9 All-cause readmissions.

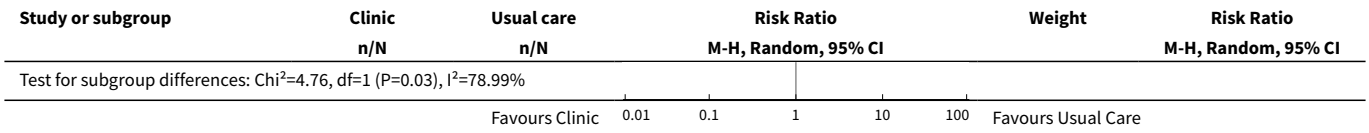
Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Cline 1998	22/56	43/80		18.86%	0.73[0.5,1.07]
Jaarsma 2008	192/340	181/339		37.41%	1.06[0.92,1.21]
Mejhert 2004	69/103	69/105		32.7%	1.02[0.84,1.24]
Thompson 2005	13/58	21/48		11.02%	0.51[0.29,0.91]
Total (95% CI)	**557**	**572**		**100%**	**0.9[0.72,1.12]**
Total events: 296 (Clinic), 314 (Usual care)					
Heterogeneity: Tau^2=0.03; Chi^2=8.59, df=3(P=0.04); I^2=65.06%					
Test for overall effect: Z=0.94(P=0.35)					



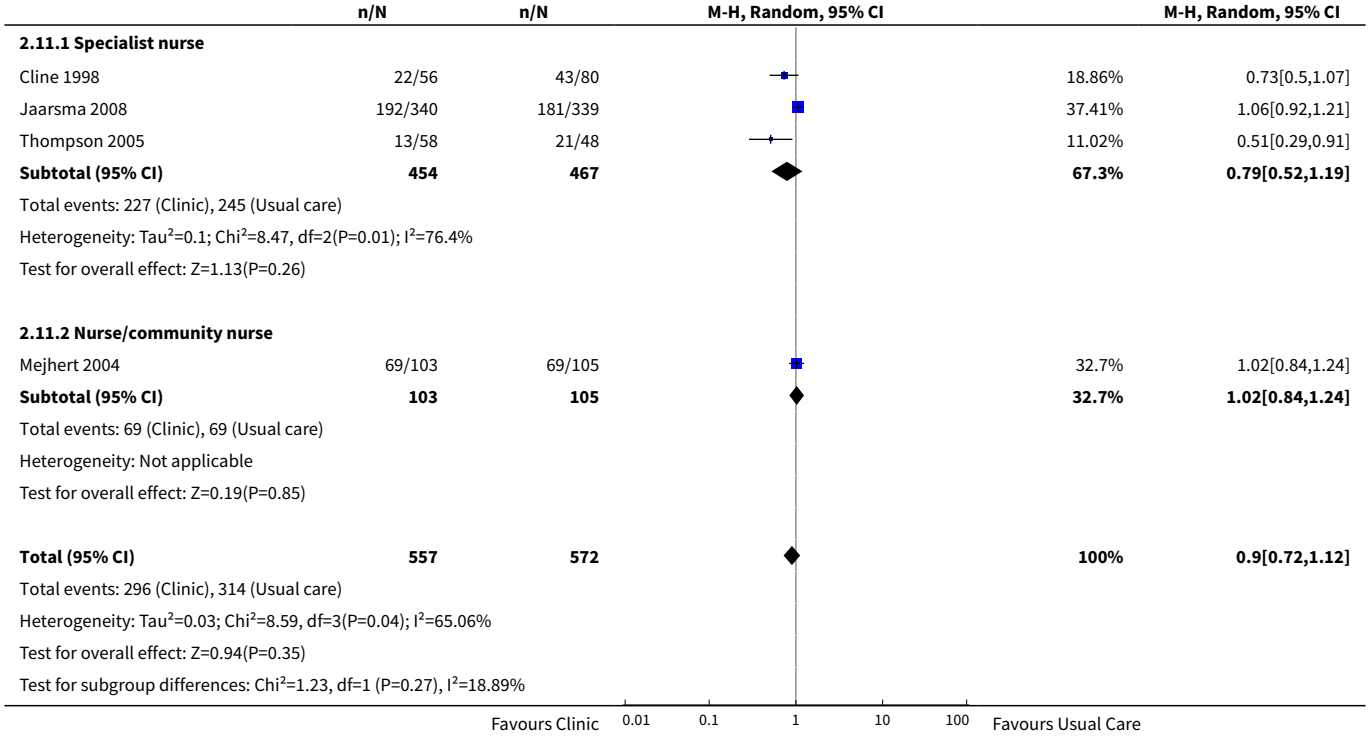
Analysis 2.10. Comparison 2 Clinic-based intervention vs usual care, Outcome 10 All-cause readmissions - subgroup analysis by length of follow-up.

Study or subgroup	Clinic n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
2.10.1 6 months' follow-up					
Thompson 2005	13/58	21/48		11.02%	0.51[0.29,0.91]
Subtotal (95% CI)	**58**	**48**		**11.02%**	**0.51[0.29,0.91]**
Total events: 13 (Clinic), 21 (Usual care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.27(P=0.02)					
2.10.2 More than 6 months' follow-up					
Cline 1998	22/56	43/80		18.86%	0.73[0.5,1.07]
Jaarsma 2008	192/340	181/339		37.41%	1.06[0.92,1.21]
Mejhert 2004	69/103	69/105		32.7%	1.02[0.84,1.24]
Subtotal (95% CI)	**499**	**524**		**88.98%**	**0.99[0.85,1.16]**
Total events: 283 (Clinic), 293 (Usual care)					
Heterogeneity: Tau^2=0.01; Chi^2=3.19, df=2(P=0.2); I^2=37.21%					
Test for overall effect: Z=0.07(P=0.94)					
Total (95% CI)	**557**	**572**		**100%**	**0.9[0.72,1.12]**
Total events: 296 (Clinic), 314 (Usual care)					
Heterogeneity: Tau^2=0.03; Chi^2=8.59, df=3(P=0.04); I^2=65.06%					
Test for overall effect: Z=0.94(P=0.35)					





Analysis 2.11. Comparison 2 Clinic-based intervention vs usual care, Outcome 11 All-cause readmissions - subgroup analysis by person delivering the intervention.



Comparison 3. Multidisciplinary vs usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 HF mortality - main analysis	2	277	Risk Ratio (M-H, Random, 95% CI)	0.46 [0.23, 0.95]
2 All-cause mortality - main analysis	8	1764	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.54, 0.83]
3 All-cause mortality - subgroup analysis by length of follow-up	8	1764	Risk Ratio (M-H, Random, 95% CI)	0.67 [0.54, 0.83]
3.1 6 months' follow-up	2	478	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.47, 1.49]
3.2 More than 6 months' follow-up	6	1286	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.49, 0.81]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 All-cause mortality - sensitivity analysis with low risk of bias	2	342	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.34, 1.25]
5 HF readmissions - main analysis	5	1108	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.50, 0.92]
6 HF readmissions - subgroup analysis by length of follow-up	5	1108	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.50, 0.92]
6.1 6 months' follow-up	2	478	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.55, 1.40]
6.2 More than 6 months' follow-up	3	630	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.44, 0.75]
7 All-cause readmissions - main analysis	5	1152	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.71, 1.01]
8 All-cause readmissions - subgroup analysis by length of follow-up	5	1152	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.71, 1.01]
8.1 6 months follow up	2	478	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.54, 1.33]
8.2 more than 6 months follow up	3	674	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.70, 1.02]
9 Quality of life - MLHFQ	2	140	Mean Difference (IV, Random, 95% CI)	-12.21 [-16.43, -7.99]

Analysis 3.1. Comparison 3 Multidisciplinary vs usual care, Outcome 1 HF mortality - main analysis.

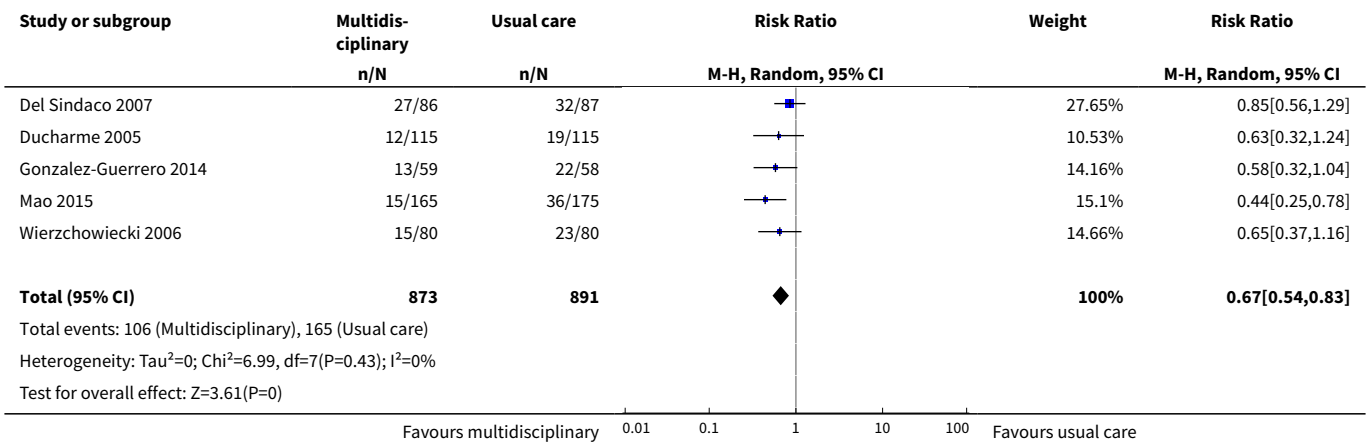
Study or subgroup	Multidisciplinary n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Gonzalez-Guerrero 2014	3/59	10/58		33.51%	0.29[0.09,1.02]
Wierzchowiecki 2006	7/80	12/80		66.49%	0.58[0.24,1.41]
Total (95% CI)	**139**	**138**		**100%**	**0.46[0.23,0.95]**
Total events: 10 (Multidisciplinary), 22 (Usual care)					
Heterogeneity: Tau^2=0; Chi^2=0.78, df=1(P=0.38); I^2=0%					
Test for overall effect: Z=2.1(P=0.04)					

Favours multidisciplinary — Favours usual care

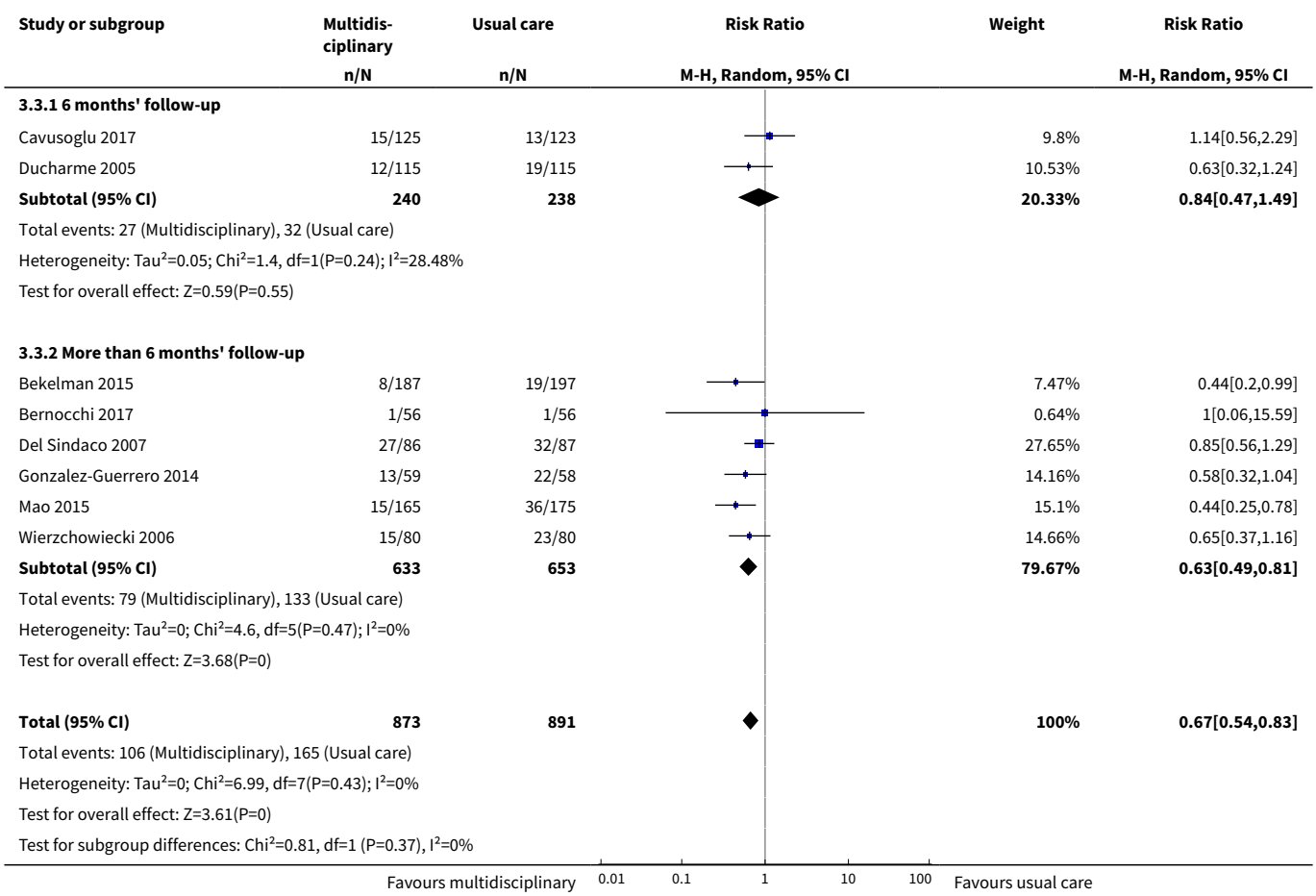
Analysis 3.2. Comparison 3 Multidisciplinary vs usual care, Outcome 2 All-cause mortality - main analysis.

Study or subgroup	Multidisciplinary n/N	Usual care n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Bekelman 2015	8/187	19/197		7.47%	0.44[0.2,0.99]
Bernocchi 2017	1/56	1/56		0.64%	1[0.06,15.59]
Cavusoglu 2017	15/125	13/123		9.8%	1.14[0.56,2.29]

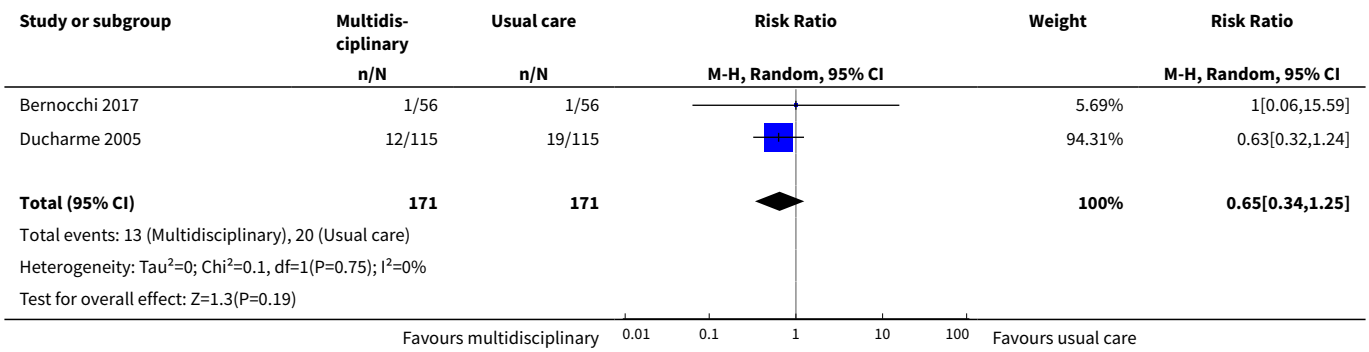
Favours multidisciplinary — Favours usual care



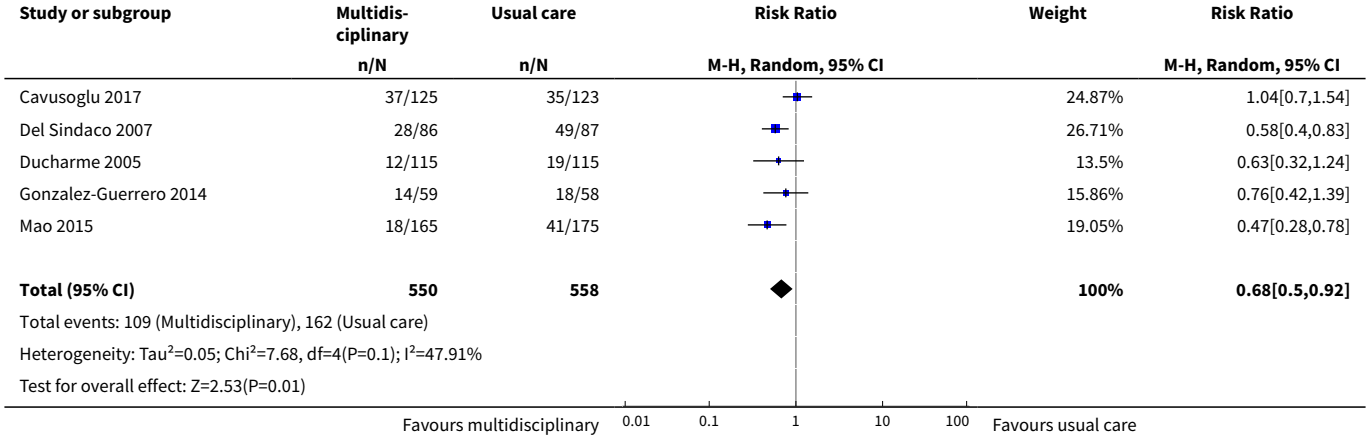
Analysis 3.3. Comparison 3 Multidisciplinary vs usual care, Outcome 3 All-cause mortality - subgroup analysis by length of follow-up.



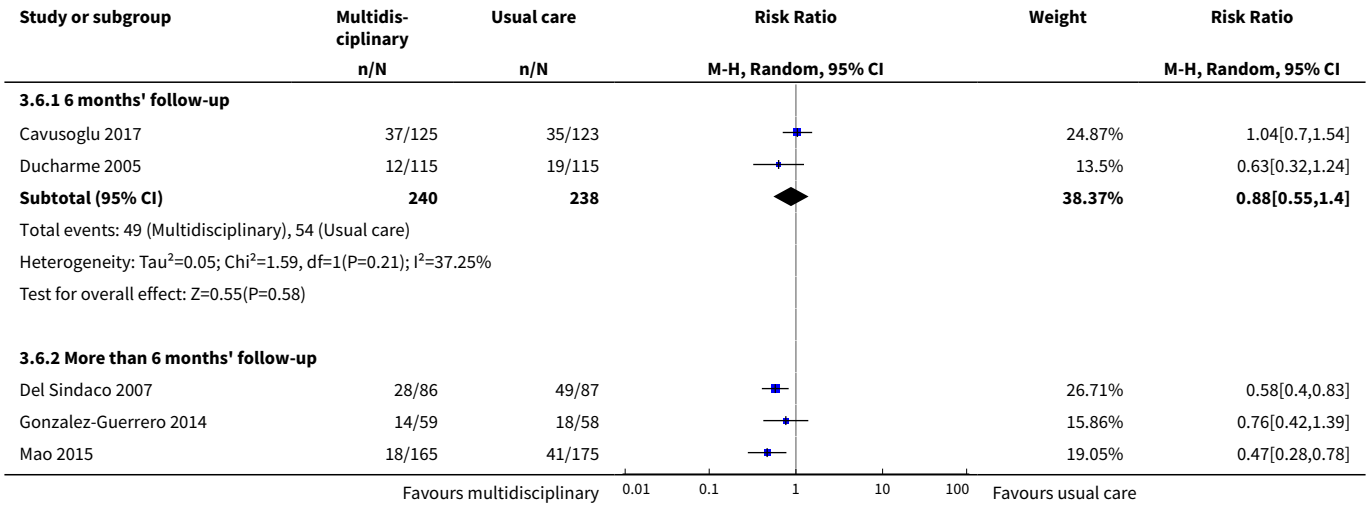
Analysis 3.4. Comparison 3 Multidisciplinary vs usual care, Outcome 4 All-cause mortality - sensitivity analysis with low risk of bias.

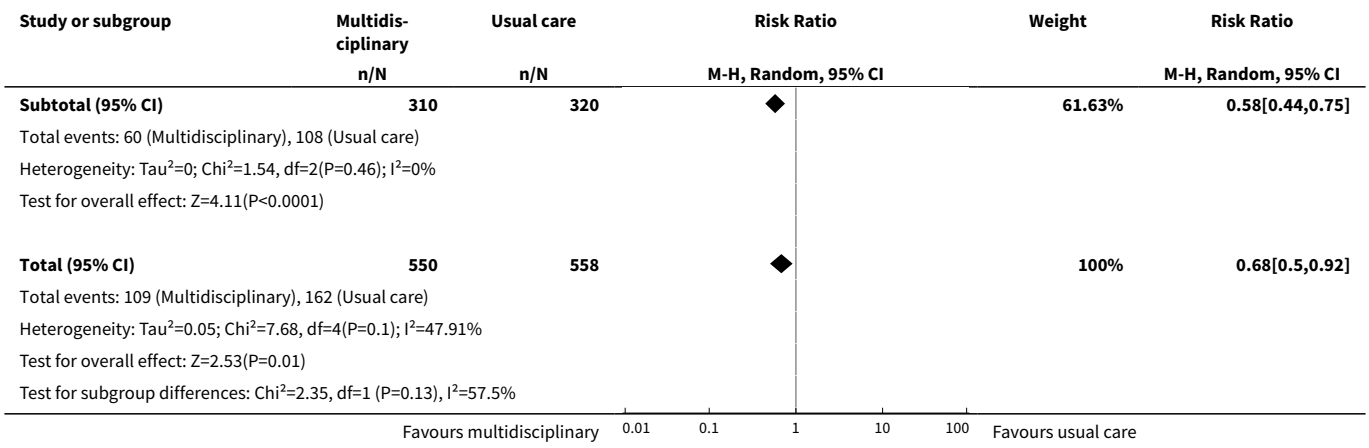


Analysis 3.5. Comparison 3 Multidisciplinary vs usual care, Outcome 5 HF readmissions - main analysis.

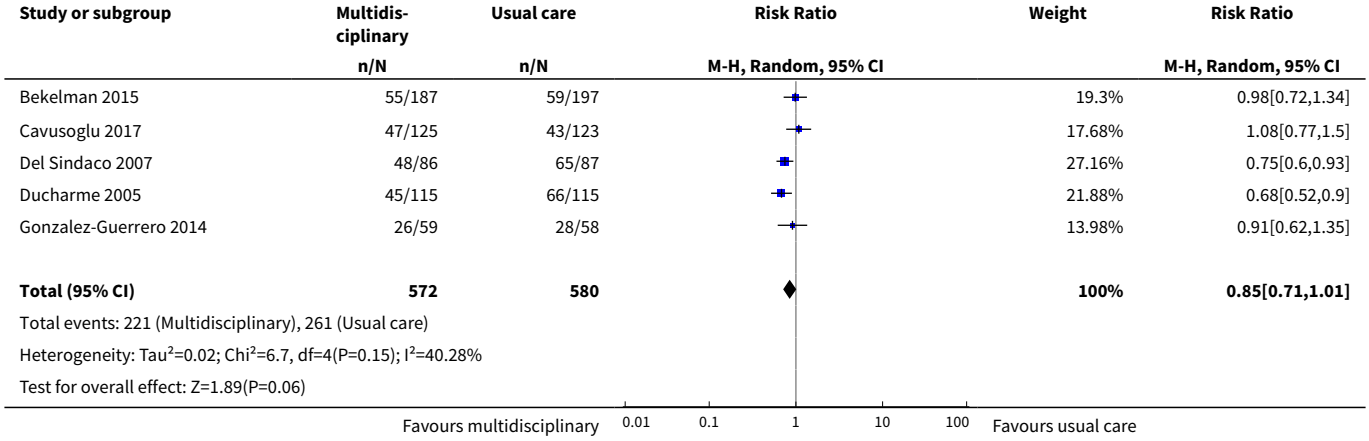


Analysis 3.6. Comparison 3 Multidisciplinary vs usual care, Outcome 6 HF readmissions - subgroup analysis by length of follow-up.

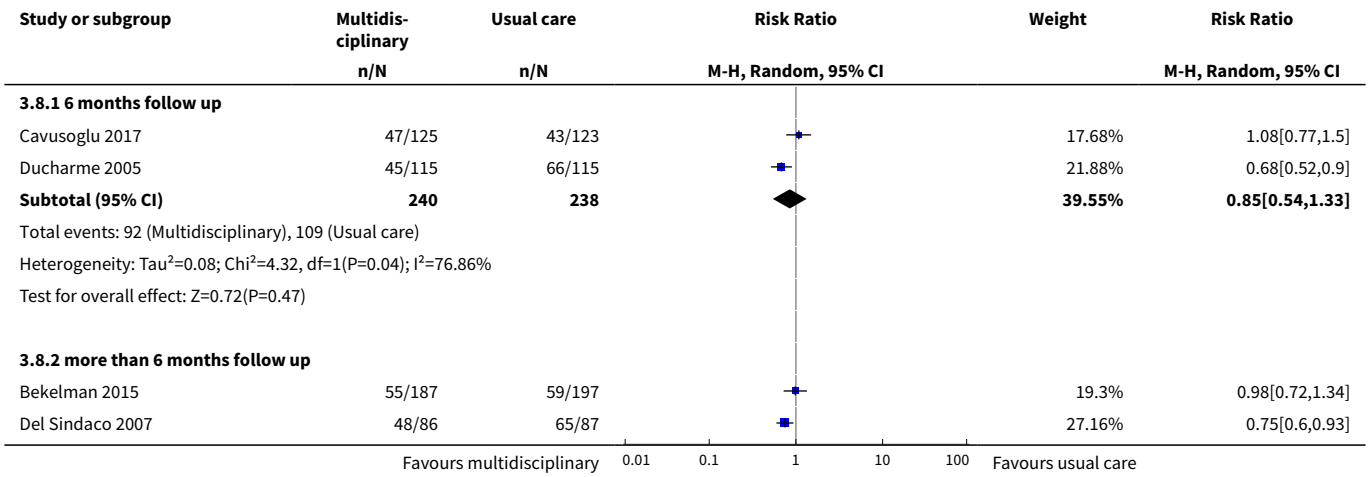


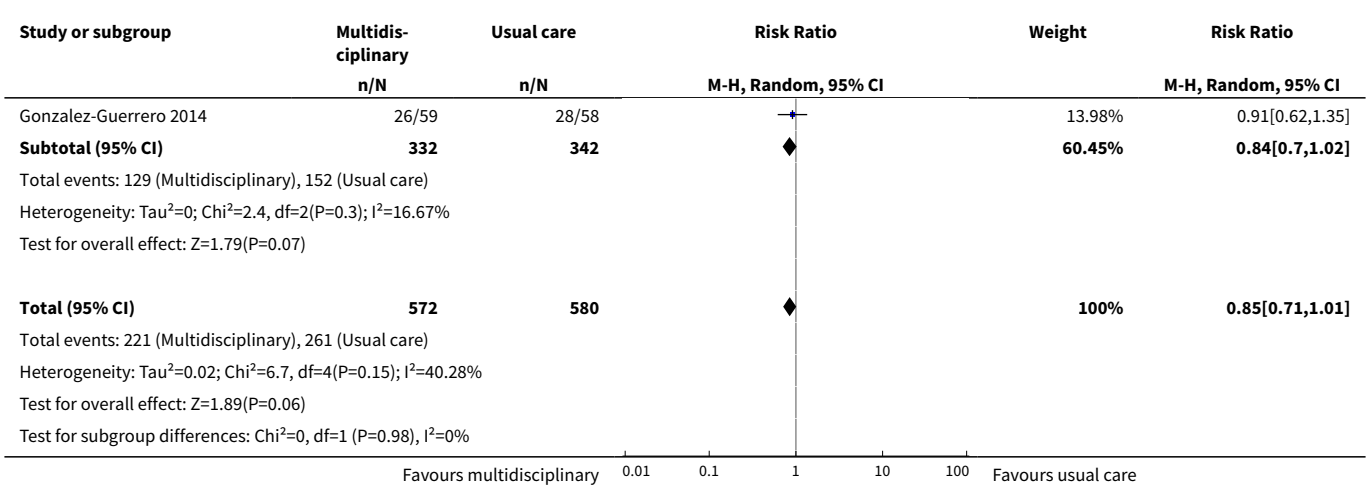


Analysis 3.7. Comparison 3 Multidisciplinary vs usual care, Outcome 7 All-cause readmissions - main analysis.

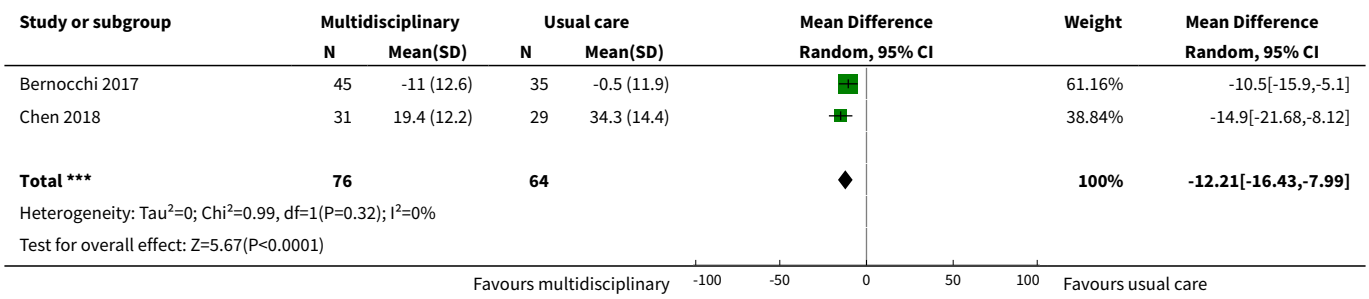


Analysis 3.8. Comparison 3 Multidisciplinary vs usual care, Outcome 8 All-cause readmissions - subgroup analysis by length of follow-up.





Analysis 3.9. Comparison 3 Multidisciplinary vs usual care, Outcome 9 Quality of life - MLHFQ.



ADDITIONAL TABLES

Table 1. Intervention components

Study	Phone follow-up	Largely educational	Self-management	Weight monitoring	Dietary advice	Exercise promotion	Medication review	Social/psychological support	Duration of intervention (may be shorter than study follow-up)
Agren 2012			Y					Y	3 months
Aldamiz-Echevarria 2007	Y	Y	Y		Y		Y		15 days
Atienza 2004	Y	Y	Y		Y	Y	Y		Median duration 509 days
Bekelman 2015	Y		Y	Y	Y		Y	Y	12 months
Berger 2010	Y		Y	Y			Y		12 months
Bernocchi 2017	Y	Y	Y		Y	Y			4 months
Blue 2001	Y	Y	Y					Y	Up to 12 months
Bohmer 2011	Y						Y		6 months
Brotons 2009	Y	Y	Y	Y			Y		12 months
Capomolla 2002		Y	Y	Y	Y	Y		Y	Not clear
Cavusoglu 2017	Y	Y	Y	Y	Y	Y	Y		6 months
Chen 2018	Y	Y	Y	Y	Y	Y	Y		6 months
Clark 2015	Y	Y	Y	Y	Y	Y	Y	Y	6 months
Cline 1998		Y	Y	Y					12 months
DeBusk 2004	Y	Y	Y	Y	Y		Y		1 year
de Souza 2014	Y	Y	Y	Y		Y	Y		4 months
Del Sindaco 2007	Y						Y		24 months

Table 1. Intervention components *(Continued)*

Doughty 2002		Y	Y	Y	Y	Y			12 months
Ducharme 2005	Y			Y	Y		Y		6 months
Dunbar 2014	Y	Y	Y	Y	Y	Y	Y		4.5 months
Gonzalez-Guerrero 2014	Y		Y		Y	Y	Y		6 months
Holland 2007		Y		Y	Y	Y			6-8 weeks
Jaarsma 2000	Y	Y							Around 1 week
Jaarsma 2008	Y (basic and intensive interventions)			Y (intensive intervention)	Y (intensive intervention)				18 months
Kasper 2002	Y			Y	Y	Y			6 months
Kimmelstiel 2004	Y	Y		Y	Y		Y		90 days + longer for unstable participants
Krumholz 2002	Y	Y							12 months
Kwok 2008	Y				Y	Y	Y	Y	6 months
Lang 2018	Y	Y	Y	Y	Y	Y		Y	12 weeks
Leventhal 2011	Y	Y	Y	Y	Y				12 months
Lopez 2006	Y	Y			Y				12 months
Mao 2015	Y	Y	Y	Y	Y	Y	Y		Intensive phase 6 months, then phone follow-up every 2-3 months; overall fol-

Table 1. Intervention components *(Continued)*

									low-up 24 months
Mehralian 2014		Y							6 months
Mejhert 2004			Y	Y	Y		Y		18 months
Naylor 2004	Y	Y	Y		Y	Y	Y		Intervention 3 months, follow-up 1 year
Nucifora 2006	Y		Y				Y		6 months
Ong 2016	Y	Y	Y	Y	Y	Y			6 months
Rainville 1999	Y			Y			Y		3 months
Salehitali 2009	Y	Y	Y	Y	Y	Y	Y		6 months
Shively 2013	Y		Y	Y	Y	Y			6 months
Stewart 1999a	Y					Y			Intervention concentrated in first 2 weeks but some phone contact up to end of follow-up (6 months)
Stromberg 2003	Y	Y	Y	Y	Y	Y	Y	Y	Unclear
Thompson 2005		Y	Y	Y					6 months
Tsuchihashi-Makaya 2013	Y	Y	Y		Y	Y		Y	6 months
Tsuyuki 2004	Y	Y	Y	Y	Y	Y			6 months
Wierzchowiecki 2006	Y	Y	Y	Y	Y	Y	Y		12 months
Yu 2015a	Y		Y	Y				Y	9 months

Table 2. Metaregression results

	All-cause mortality		All-cause readmissions		HF readmissions	
Intervention component	Ratio of RR	P value	Ratio of RR	P value	Ratio of RR	P value
Phone follow-up	0.72 (0.37 to 1.38)	0.31	n/a	n/a	n/a	n/a
Largely educational	1.16 (0.80 to 1.68)	0.42	0.93 (0.71 to 121)	0.53	0.65 (0.46 to 0.93)	0.02
Self-management	1.03 (0.72 to 1.46)	0.87	1.05 (0.81 to 1.36)	0.68	0.72 (0.48 to 1.07)	0.09
Weight management	0.96 (0.68 to 1.35)	0.81	1.32 (1.09 to 1.60)	0.008	1.53 (1.07 to 2.18)	0.03
Dietary advice	0.95 (0.67 to 1.35)	0.78	1.15 (0.89 to 1.48)	0.26	1.29 (0.76 to 2.18)	0.31
Exercise promotion	0.93 (0.66 to 1.30)	0.65	0.95 (0.75 to 1.19)	0.61	0.89 (0.55 to 1.45)	0.61
Medication review	0.86 (0.62 to 1.20)	0.36	0.86 (0.71 to 1.03)	0.09	0.78 (0.50 to 1.22)	0.25
Social/psychological support	0.98 (0.59 to 1.61)	0.92	0.92 (0.68 to 1.26)	0.58	0.76 (0.40 to 1.43)	0.35

HF: heart failure; **RR:** risk ratio
Phone follow-up was dropped from the model for all-cause readmissions and HF readmissions due to collinearity, so we could not calculate ratio of RR or P value.

APPENDICES

Appendix 1. Search strategies January 2018

CENTRAL via CRS Web

#1MeSH descriptor: [Heart Failure] explode all trees
#2((heart* or cardiac* or myocard*) near2 (fail* or insuff*))
#3(heart* near2 decomp*)
#4#1 or #2 or #3
#5MeSH descriptor: [Disease Management] this term only
#6(disease* near5 manag*)
#7MeSH descriptor: [Patient Care Management] this term only
#8MeSH descriptor: [Medication Therapy Management] this term only
#9MeSH descriptor: [Patient Care Team] explode all trees

#10MeSH descriptor: [Patient-Centered Care] this term only
#11(patient* near3 manag*)
#12(patient* near4 (care or caring))
#13(deliver* near2 care)
#14(manag* near5 care)
#15(management near5 program*)
#16(case near5 manag*)
#17MeSH descriptor: [Home Care Services] this term only
#18MeSH descriptor: [Home Care Services, Hospital-Based] this term only
#19(home near5 (intervention* or care))
#20(home near visit*)
#21homecare
#22MeSH descriptor: [Ambulatory Care] this term only
#23(ambulatory near2 (care or caring))
#24MeSH descriptor: [Patient Discharge] this term only
#25(discharg* near5 program*)
#26(practice next guideline*)
#27MeSH descriptor: [Practice Guidelines as Topic] this term only
#28(comprehensive* near5 (care or caring))
#29multidisciplinary
#30(treatment* near5 plan*)
#31(nurse* next led)
#32(discharg* near5 plan*)
#33#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32
#34#4 and #33

MEDLINE Ovid

1. exp Heart Failure/
2. ((heart* or cardiac* or myocard*) adj2 (fail* or insuff*)).tw.
3. (heart* adj2 decomp*).tw.
4. or/1-3
5. disease management/
6. (disease* adj5 manag*).tw.
7. Patient Care Management/
8. Medication Therapy Management/
9. exp Patient Care Team/
10. Patient-Centered Care/
11. (patient* adj3 manag*).tw.
12. (patient* adj4 (care or caring)).tw.
13. (deliver* adj2 care).tw.
14. (manag* adj5 care).tw.
15. ((management or care) adj5 program*).tw.
16. (case adj5 manag*).tw.
17. Home Care Services/
18. Home Care Services, Hospital-Based/
19. (home adj5 (intervention* or care)).tw.
20. (home adj visit*).tw.
21. homecare.tw.
22. Ambulatory Care/
23. (ambulatory adj2 (care or caring)).tw.
24. Patient Discharge/
25. (discharg* adj5 program*).tw.
26. (practice adj guideline*).tw.
27. Practice Guidelines as Topic/
28. (comprehensive* adj5 (care or caring)).tw.
29. multidisciplinary.tw.
30. (treatment* adj5 plan*).tw.
31. (nurse* adj5 led).tw.
32. (discharg* adj5 plan*).tw.
33. or/5-32

34. 4 and 33
35. randomized controlled trial.pt.
36. controlled clinical trial.pt.
37. randomized.ab.
38. placebo.ab.
39. clinical trials as topic.sh.
40. randomly.ab.
41. trial.ti.
42. 35 or 36 or 37 or 38 or 39 or 40 or 41
43. exp animals/ not humans.sh.
44. 42 not 43
45. 34 and 44

Embase Ovid

1. exp heart failure/
2. ((heart* or cardiac* or myocard*) adj2 (fail* or insuff*)).tw.
3. (heart* adj2 decomp*).tw.
4. or/1-3
5. disease management/
6. (disease* adj5 manag*).tw.
7. patient care/
8. medication therapy management/
9. (patient* adj3 manag*).tw.
10. (patient* adj4 (care or caring)).tw.
11. (deliver* adj2 care).tw.
12. (manag* adj5 care).tw.
13. ((management or care) adj5 program*).tw.
14. (case adj5 manag*).tw.
15. home care/
16. (home adj5 (intervention* or care)).tw.
17. (home adj visit*).tw.
18. homecare.tw.
19. ambulatory care/
20. (ambulatory adj2 (care or caring)).tw.
21. hospital discharge/
22. (discharg* adj5 program*).tw.
23. (practice adj guideline*).tw.
24. (comprehensive* adj5 (care or caring)).tw.
25. multidisciplinary.tw.
26. (treatment* adj5 plan*).tw.
27. (nurse* adj5 led).tw.
28. (discharg* adj5 plan*).tw.
29. or/5-28
30. 4 and 29
31. random$.tw.
32. factorial$.tw.
33. crossover$.tw.
34. cross over$.tw.
35. cross-over$.tw.
36. placebo$.tw.
37. (doubl$ adj blind$).tw.
38. (singl$ adj blind$).tw.
39. assign$.tw.
40. allocat$.tw.
41. volunteer$.tw.
42. crossover procedure/
43. double blind procedure/
44. randomized controlled trial/
45. single blind procedure/
46. 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45
47. (animal/ or nonhuman/) not human/

48. 46 not 47
49. 30 and 48
50. limit 49 to embase

CINAHL

S53 S51 AND S52
S52 EM 20140212-20180109
S51 S32 AND S50
S50 S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49
S49 TX cross-over*
S48 TX crossover*
S47 TX volunteer*
S46 (MH "Crossover Design")
S45 TX allocat*
S44 TX control*
S43 TX assign*
S42 TX placebo*
S41 (MH "Placebos")
S40 TX random*
S39 TX (doubl* N1 mask*)
S38 TX (singl* N1 mask*)
S37 TX (doubl* N1 blind*)
S36 TX (singl* N1 blind*)
S35 TX (clinic* N1 trial?)
S34 PT clinical trial
S33 (MH "Clinical Trials+")
S32 S4 AND S31
S31 S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30
S30 (discharg* N5 plan*)
S29 (nurse* N2 led)
S28 (treatment* N5 plan*)
S27 multidisciplinary
S26 (comprehensive* N5 (care or caring))
S25 (practice N2 guideline*)
S24 (discharg* N5 program*)
S23 (MH "Patient Discharge")
S22 (ambulatory N2 (care or caring))
S21 (MH "Ambulatory Care")
S20 homecare
S19 (home N4 visit*)
S18 (home N5 (intervention* or care))
S17 (MH "Shared Services, Health Care")
S16 (MH "Home Health Care")
S15 (case N5 manag*)
S14 ((management or care) N5 program*)
S13 (manag* N5 care)
S12 (deliver* N2 care)
S11 (patient* N4 (care or caring))
S10 (patient* N3 manag*)
S9 (MH "Patient Centered Care")
S8 (MH "Multidisciplinary Care Team")
S7 (MH "Patient Care Plans+")
S6 (disease* N5 manag*)
S5 (MH "Disease Management")
S4 S1 OR S2 OR S3
S3 (heart* N2 decomp*)
S2 ((heart* or cardiac* or myocard*) N2 (fail* or insuff*))
S1 (MH "Heart Failure+")

DARE via Cochrane Library

#1MeSH descriptor: [Heart Failure] explode all trees
#2((heart* or cardiac* or myocard*) near/2 (fail* or insuff*))
#3(heart* near/2 decomp*)
#4#1 or #2 or #3
#5MeSH descriptor: [Disease Management] this term only
#6(disease* near/5 manag*)
#7MeSH descriptor: [Patient Care Management] this term only
#8MeSH descriptor: [Medication Therapy Management] this term only
#9MeSH descriptor: [Patient Care Team] explode all trees
#10MeSH descriptor: [Patient-Centered Care] this term only
#11(patient* near/3 manag*)
#12(patient* near/4 (care or caring))
#13(deliver* near/2 care)
#14(manag* near/5 care)
#15(management near/5 program*)
#16(case near/5 manag*)
#17MeSH descriptor: [Home Care Services] this term only
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#19(home near/5 (intervention* or care))
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#22MeSH descriptor: [Ambulatory Care] this term only
#23(ambulatory near/2 (care or caring))
#24MeSH descriptor: [Patient Discharge] this term only
#25(discharg* near/5 program*)
#26(practice next guideline*)
#27MeSH descriptor: [Practice Guidelines as Topic] this term only
#28(comprehensive* near/5 (care or caring))
#29multidisciplinary
#30(treatment* near/5 plan*)
#31(nurse* next led)
#32(discharg* near/5 plan*)
#33#5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32

Clinicaltrials.gov

Condition or disease: “heart failure”
Other: randomized
Intervention/treatment: (“disease management” OR “self care”) AND (other OR behavioral)
Applied filters: interventional, adult, older adult

ICTRP

heart failure AND disease management AND random*

WHAT'S NEW

Date	Event	Description
3 October 2018	New citation required but conclusions have not changed	22 new studies added. Conclusions unchanged but findings now more robust due to increased number of studies and participants.
2 October 2018	New search has been performed	We re-ran the searches on 9 January 2018.

HISTORY

Protocol first published: Issue 4, 2000
Review first published: Issue 2, 2005

Date	Event	Description
23 December 2011	New citation required and conclusions have changed	Updated with results of new searches. 16 new studies included, and 10 from the original review removed as not meeting revised inclusion criteria. Change in authorship reflects changes in team over time
8 September 2008	Amended	Converted to new review format
1 February 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

AT is guarantor of the review.

ST, and AT conceived and designed this update.

ST, NM and AT screened search results against inclusion criteria and carried out data extraction.

AT and NM appraised the risk of bias and GRADE rating of included studies.

AT wrote to authors of papers for additional information.

AT managed the data for the review, entered the data into Review Manager 5 (Review Manager 2014) and analysed the data.

AT and NM wrote the review, with ST and RT providing methodological perspective, clinical perspective and general advice.

DECLARATIONS OF INTEREST

AT: none known

NM: none known

RT: none known

ST: none known

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

No protocol was published for this update, so we are including differences between the last update (Takeda 2012) and the current update.

Changes in authorship have taken place since the protocol was registered, since two new researchers (AT, NM) joined the team and others have moved on to other fields.

- The title of this review has been changed from 'Clinical Service Organisation for Heart Failure' to reflect changes in terminology, with an emphasis on disease management programmes rather than organisation of services.
- The objective of the review has been simplified by merging the original primary and secondary objectives into one.
- The original review contained four different mortality outcomes and four different readmission outcomes as primary outcomes, and four secondary outcomes. For this update, we amended these to simplify the review and focus on user-important outcomes.

INDEX TERMS

Medical Subject Headings (MeSH)

Aftercare [*organization & administration]; Case Management [*organization & administration]; Cause of Death; Chronic Disease; Health Status; Heart Failure [mortality] [*therapy]; Length of Stay; Patient Readmission [*statistics & numerical data]; Practice Patterns, Nurses' [organization & administration]; Quality of Life; Randomized Controlled Trials as Topic

MeSH check words

Aged; Aged, 80 and over; Humans